The American Society of Hospital Pharmacists, an affiliate of the American Pharmaceutical Association, is a national organization devoted to the profession of hospital pharmacy and dedicated to the improvement of pharmaceutical service in the interest of better patient care in hospitals.

MEMBERSHIP in the American Society of Hospital Pharmacists and the American Pharmaceutical Association is open to all practicing hospital pharmacists. With membership are included subscriptions to the American Journal of Hospital Pharmacy and to the *Journal* of the American Pharmaceutical Association, Pract. Pharm. Ed., as well as the several services of each organization.

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American Journal of Hospital Pharmacy

American Society of Hospital Pharmacists

VOLUME 15 NUMBER 3 MARCH 1958

articles

departments

as the president sees it—

LEO F. GODLEY, *Bronson Methodist Hospital, Kalamazoo, Michigan*

Here in Kalamazoo we've been experiencing a harsh winter with a total snow fall of something more than 80 inches. This makes traveling a bit slow and hazardous; but it created a sort of Christmas card setting for the Executive Committee meeting the last of January. The Upjohn Company let us use their beautiful country conference facility, Brook Lodge. There we met Thursday night, all day Friday, all day and evening on Saturday, and Sunday morning. We did a great deal of work with a very crowded agenda. We had a lot of fun too.

Mr. Joseph Oddis, Dr. William Heller, and Dr. Robert Fischelis were with us for the entire meeting. They were invited to help us in specific areas of SOCIETY interest and we appreciated and enjoyed their participation and contributions.

I guess we were the first to know about the H.A.K. Whitney Award winner for 1958. I believe that Walter Frazier gave his official acceptance to Clifton Latiolais at Brook Lodge. Clif is the Michigan Society's Whitney Award Committee Chairman. Hospital pharmacists from all over the nation will be proud to see Pharmacist Frazier receive this high honor.

I met with the Michigan Chapter in Detroit in Mid-January. It was a pleasure seeing so many old friends from around Detroit again. I had a chance to talk over the AMERICAN JOURNAL OF HOSPITAL PHARMACY with Don Francke. He gave me a copy of the front cover to show to the group that night. Speaking of the JOURNAL, Bill Heller stopped by Hamilton Press on the way to the Executive Committee meeting and brought copies of the January issue. We had a great time discussing it and romancing over the significance of this particular point in SOCIETY history. It must be a lucid and interesting view that Editor Francke sees with nearly 15 years of Bulletin editorship.

This Executive Committee meeting pointed out to us very vividly that the approaching annual convention is going to be one of exciting interest—the Special Committees, the JOURNAL, the Formulary Service, Research and Development, Constitution and By-Laws, Whitney Award, international programs, Affiliated Chapters.

Meeting in Washington with the ASHP-AHA Joint Committee on January 31 was a rewarding experience. It seemed that we made several decisions and recommendations on questions that had been on the committee's agenda for some time. It is satisfying, indeed, to work with other organizations, for here the feeling of universal contact and influence is keenly felt; and that's why, of course, related organization cooperation is important. I look forward to our expected work with the National League of Nursing with a great deal of enthusiasm. I am sure that the contact will broaden our experience and increase our perception of service.

We enjoyed meeting and working with Mr. C. P. Cardwell, the new AHA representative on the Joint Committee. Mr. Cardwell is Administrator of the Medical College of Virginia Hospital and replaces Dr. August Groeschel. We regret the loss of Dr. Groeschel to the Committee, but I am sure that we can feel free to call upon the wisdom and experience of Dr. Groeschel anyway.

The North Carolina Society of Hospital Pharmacists asked me to meet with them in Charlotte in early February. It was particularly enjoyable for me since I am a South Carolinian and there were a few of my countrymen there. Dean Robert Morrison of my Alma Mater, The University of South Carolina, College of Pharmacy was there; and I was most pleased and flattered. It was good seeing old friends again, and making new ones in a section of the country that I recall so pleasantly. Tom Reamer called long distance from Durham just before I was called on to address the group; and that was all that was needed to make it a perfect day. I was sorry that I could not stay over an extra day to accept Dean Morrison's invitation to talk with his 17 students in Hospital Pharmacy. I noted in passing that the icy finger of Winter had touched the South too.

I had a nice chat with President-Elect Bogash and he is enthusiastically looking forward to the new SOCIETY year. He was quite deliberately indoctrinated at the Brook Lodge Executive Committee meeting. I am sure that the SOCIETY will flourish under his leadership.

I had a very interesting meeting last week with the Illinois Chapter. They met in Chicago and Mr. Ed Duncan of the Public Health Service moderated a panel which consisted of Joseph Oddis of the AHA, Fred Mehaffey of the NABP, and myself. We discussed our respective organizations and had a real fine time, at least I did. While I was in Chicago, Mr. Oddis took me through the AHA headquarters where we spoke briefly with Dr. LeRoy Bates, Secretary of the Council on Professional Practice, and then he showed me the future home of the AHA which is just a few blocks away. It is now just an impressive organized skeleton of bare steel and concrete; but with a little imagination, their new home takes on a very comfortable and adequate appearance.

Leo F. Godley

News

F.I.P. Congress of Pharmaceutical Sciences

The 18th Congress of Pharmaceutical Sciences organized by the Scientific Section of the International Pharmaceutical Federation will be held in Brussels, Belgium, September 8 to 14, 1958. Authors who wish to present a scientific paper are requested to send the title of their presentation, together with an abstract of 200 to 300 words, to Professor J. Thomas, Secretary of the Congress, Institute of Pharmacy, 50 Avenue F. D. Roosevelt, Brussels, Belgium, before May 1, 1958. The time allotted to a single presentation will not exceed 20 minutes, in order that each paper may have an appropriate discussion.

Papers submitted should represent original work not yet published. They will be submitted for consideration by a special committee of the Scientific Section and, when accepted, will be assigned to an appropriate session.

The following is the general program outline for the Congress of Pharmaceutical Sciences:

MONDAY 8 SEPTEMBER
11:00 A.M. Opening of the Congress and Plenary Assembly.
Award of the Höst-Madsen Medal
2:30 P.M. General Assembly of the Congress of Pharmaceutical Sciences.
Presentation of 2 or 3 general papers.

TUESDAY 9
9:30 A.M. and
2:00 P.M. Symposium on Radioisotopes and their applications.
5:00 P.M. Meeting of the Scientific Section.

WEDNESDAY 10
9:30 A.M. F.I.P. General Assembly.
2:00 P.M. Symposium on Biological Measurements and Their Applications.
5:30 P.M. Joint Meeting of the Scientific Section and the Section on Press and Documentation.
Discussion on Pharmaceutical Abstracts.

THURSDAY 11
9:30 A.M. and
2:00 P.M. Presentation of Scientific Papers.

FRIDAY 12
Visit to the World's Exposition.

SATURDAY 13
9:30 A.M. Scientific Communications and Discussions.
2:30 P.M. F.I.P. General Assembly.
Presentation of Reports from the Scientific Section.

The 18th International Congress of Pharmaceutical Sciences will be held in conjunction with the General Assembly of the Fédération Internationale Pharmaceutique during the week of September 8 in Brussels, Belgium.

A.M.A.—A.Ph.A.—N.A.R.D. Committees Review Problems

Broad discussions of a wide variety of subjects affecting relations between the medical and pharmaceutical professions featured the meeting of the Pharmacy Liaison Committee of the Board of Trustees of the American Medical Association with the National Pharmacy Committee on Relations with the Health Professions at the Palmer House, Chicago, on Thursday, February 6.

The session was under the chairmanship of Dr. Julian Price, member of the A.M.A. Board of Trustees and Chairman of the Pharmacy Liaison Committee. Others in attendance representing the A.M.A. were Dr. Leonard W. Larson and Dr. James Z. Appel, of the A.M.A. Board of Trustees and C. Joseph Stetler, Director of the A.M.A. Law Department.

All of the National Pharmacy Committee members were in attendance. They include Frank W. Moudry, Past President; Willard B. Simmons, Chairman of the Executive Committee; Mearl Pritchard, and Harry J. Towers, Manager, all representing the N.A.R.D.; and Ronald V. Robertson, Chairman of the Committee on Professional Relations; John B. Heinz, Chairman of the Council and Robert P. Fischelis, Secretary and General Manager, all representing the A.Ph.A.

A frank exchange of views on legislation affecting the two professions indicated that there is general agreement on the need for very careful study of the medical care problems of the aged. This is considered to be a long-range project because of the necessity for further research and study.

The joint committees were in agreement that the medical aspects of the Forand Bill were objectionable. However, a need exists for devising acceptable alternatives.

A review of the Jenkins-Keogh Bills indicated that their provisions for enabling self-employed members of the health professions to provide the equivalent of Social Security pensions for themselves are worthy of support from the health professions.

Discussion of the present procedure of paying pharmacists for prescription and other pharmacy services, through the physician, under the Medicare program, revealed that neither the medical nor the pharmaceutical profession is satisfied with the present arrangement. Both professions believe that any program for furnishing drugs and pharmaceutical services under this program should be set up to provide payment by the government directly to the dispensing agent.

Considerable time was spent in discussion of more satisfactory means for meeting the problem of distribution of drugs in scarce supply when such situations arise as had to be faced in connection with distribution of poliomyelitis vaccine and Asian Influenza vaccine. It was the consensus of the joint meeting that state and local medical and pharmaceutical associations be encouraged to organize to handle such situations at the local level.

It was also decided that efforts be made to have the practitioners of medicine and pharmacy, who must be relied on to administer and supply new and temporarily scarce drugs, represented in conferences between government agencies and producers of drugs, in the early stages of distribution of such new and temporarily scarce drugs, so as to avoid situations such as have arisen in the past.

Other topics considered at this meeting included self-medication, physician-owned pharmacies, labeling of prescriptions with the names of ingredients, and professional supervision over the distribution of drugs through various channels. It was recognized that most of these matters must be handled by state and local associations and much emphasis was placed upon an early implementation of the program to organize joint committee meetings of physicians and pharmacists at state and local levels.

National Pharmacy Week Contest Winners

One of the highlights of the annual observance of National Pharmacy Week is the display contest which is divided into four areas of competition. These are: retail pharmacy, public exhibits, pharmacy colleges, hospitals and clinics.

The A.Ph.A. Committee on Public Relations which sponsors National Pharmacy Week met in Washington, D.C. early in January to judge a record number of photographs entered in the 1957 display contest. The winners they selected will receive appropriate awards at the First General Session of the A.Ph.A. Convention in Los Angeles, California the week of April 20, 1958.

Members of the Committee on Public Relations include J. Warren Lansdowne, Chairman, of Indianapolis; George A. Bender of Detroit; John A. Lynch of Philadelphia; George F. Archambault and Robert P. Fischelis of Washington, D. C.

The Committee selections for the 1957 National Pharmacy Week Display Contest awards are as follows:

Retail Pharmacy Awards: The First Prize of $200 and a plaque is awarded to Stanley Bishop, California Avenue Pharmacy, 392 California Ave., Palo Alto, California.

The Second Prize of $100 and a plaque is awarded to John Stadnik, Miami Springs Pharmacy, P.O. Box 615, Miami Springs, Florida.

The Third Prize of $50 and a plaque is awarded to Henry H. Gregg, Gregg's Pharmacy, 4954 France Ave., So., Minneapolis 10, Minnesota.

The following were awarded certificates of merit for displays in the retail pharmacy competition:

Morris G. Goldstein, Service Pharmacy, 826 - 17th St., N.W., Washington, D.C.; Russell H. Miesse, Miesse Pharmacy, 1686 E. Main St., Columbus, Ohio; James E. Sinclair, O'Dell Drugs, 10 S. Main St., Clarkston, Michigan.

Pharmacy College Awards. The First Prize, consisting of a plaque is awarded to Temple University School of Pharmacy, Philadelphia, Pa.

The Second Prize, consisting of a certificate of merit, is awarded to the A.Ph.A. Student Branch at the New England College of Pharmacy, Boston, Mass.

The Third Prize, consisting of a certificate of merit, is awarded to the A.Ph.A. Student Branch at the Massachusetts College of Pharmacy, Boston, Mass.

Public Exhibit Awards. The First Prize, consisting of a plaque, is awarded to the Fresno-Madera County Branch of the A.Ph.A., Fresno, California.

The Second Prize, consisting of a certificate of merit is awarded to the School of Pharmacy at Oregon State College, Corvallis, Oregon.

The Third Prize, consisting of a certificate of merit, is awarded to the Gamma Upsilon Chapter of Kappa Psi Fraternity at the University of Arizona, Tucson, Arizona.

Hospitals and Clinics Awards. The First Prize, consisting of a plaque, is awarded to Robert Simons, The Memorial Hospital, Wilmington, Delaware, for his display in this hospital.

The Second Prize, consisting of a certificate of merit, is awarded to Sister Mary Oswalda, St. Joseph's Children's and Maternity Hospital, Scranton, Pennsylvania, for her display in this hospital.

The Third Prize, consisting of a certificate of merit, is awarded to J. Svihra, Jr., Perth Amboy General Hospital, Perth Amboy, New Jersey, for his display in this hospital.

Philadelphia Offers Four Special Summer Courses

During the summer of 1958, four special courses for practicing scientists will be available at the Philadelphia College of Pharmacy and Science. Three courses dealing with radioisotopes will comprise the Fifth Annual Radiochemical Institute to be offered by the College, and one course in the Preparation of

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News

Parenteral Products will be available for pharmacists through the cooperation of the Philadelphia Hospital Pharmacists' Association.

The radiochemical courses, under the direction of Dr. Arthur Osol and Dr. Grafton D. Chase of the College, will be given by fifteen faculty members and guest lecturers. From July 7 thru 18, there will be a two-week introductory course for individuals with a basic science background but no previous experience with radioisotopes. From July 21 thru 25, there will be a one-week advanced course for individuals with a background of course number 1 or its equivalent, and this will deal with the biological and medical applications of radioisotopes. From July 28 through August 1 there will be another advanced course of one week's duration dealing with radiochemical instrumentation. Enrollment in each of these three courses is limited to thirty participants.

The fourth course during the summer, to be conducted by Dr. Kenneth E. Avis, of the College faculty, on the Preparation of Parenteral Products, will be offered from July 7 thru July 18. This course is open to all persons with previous training and experience in pharmacy, either in hospital work or otherwise. The enrollment in this course, too, is limited. Further details and application forms may be obtained from the Registrar of the Philadelphia College of Pharmacy and Science, 43rd. Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pennsylvania.

A.Ph.A. Membership Reaches New High

For the first time in the history of the American Pharmaceutical Association, we have passed the 30,000 mark in total membership.

In his inaugural address at the 1948 convention in San Francisco, A.Ph.A. President Ernest Little recommended that a goal of not less than 30,000 members be set for the Association's Centennial year (1952). The House of Delegates passed a resolution to that effect. There has been a steady increase in total membership each year since 1944, although there was a decrease in active membership in 1955, when dues were increased from $10 to $15. This decrease was partly recovered in 1956, and at the end of 1957 the Association had 1411 more active members than ever before.

At the close of the calendar year 1957, there were 17,832 active and 12,256 associate (student) members, or a total of 30,088. This is an increase of 1300 over the largest total membership ever reported before at the close of a fiscal year.

In 1956 the total membership reached 28,788, of which 15,976 were active members and 12,812 were associate (student) members.

The net gain in active membership for the year 1957 amounted to 1856.

A.M.A. Drafts New Law to Cut Poison Deaths

After a 15 months' study, the Committee on Toxicology of the American Medical Association has announced that it has formulated a broad and encompassing model law for the precautionary labeling of hazardous substances in commercial, household, and industrial chemical products.

Speaking before the Section on Food, Drug & Cosmetic Law of the New York Bar Association January 29, Bernard E. Conley, Ph.D., Chicago, Secretary of the A.M.A. committee, said the proposed legislation is intended as a model for uniform laws to require declaration of hazardous ingredients and warning statements on the label and in the accompanying literature of chemical products used in the home and elsewhere.

"The proposed model law," Conley said, "was drafted after an exhaustive review of existing statutes revealed a hodge-podge of local regulations for the labeling of chemicals."

The law is directed against those hazardous substances defined as toxic, irritating, sensitizing, corrosive, flammable, explosive, or radioactive under customary or reasonably anticipated conditions of handling and use.

The law, as drafted by the A.M.A. committee headed by Dr. Torald Sollman, Cleveland, Ohio, would:

(1) Require the labeling of all chemical products containing hazardous substances which are not now regulated.

(2) Require the same labeling standards to apply to chemicals for export as those for domestic consumption, thereby obviating the common complaint that less-than-standard products are sold to foreign customers.

(3) Prohibit re-use of food and drug containers bearing their original labels.

(4) Require identification and warnings for strongly sensitizing chemicals which cause allergic or inflammatory reactions in living tissue on contact.

Conley said a significant departure in drafting the new law was deletion of the word "poison" from the bill's provisions. This decision was reached, he said,

after surveys showed a wide variation in existing legal limits for poison and a lack of agreement among scientists on a definition of the term.

"The A.M.A. committee," he said, "feels that reference standards for toxicity based on animal tests provide a more consistent and reliable index of the poisonous properties of chemicals."

The committee's work had strong support not only from the chemical industry but also from the National Drug Trade Conference and the American Public Health Association.

Conley told the bar association that inadequate labeling of potentially harmful chemicals has been a major handicap to a successful attack on the problem of accidental poisoning.

"Lack of information about hazardous ingredients in certain emergencies," he said, "may enhance the gravity by complicating or delaying treatment."

The A.M.A. official said the latest mortality statistics show that 1,431 persons died from accidental overexposure to packaged chemicals in 1955. "One-quarter of these fatal accidental poisonings by liquid and solid substances occurred in pre-school age children and over 80 percent occurred in the home. Non-fatal poisonings are estimated to be 100 to 150 times the number of fatalities," he said, adding:

"And these are impressive statistics for a cause of injury and death which is considered to be largely preventable."

Conley said that while tremendous strides have been made in recent years in reducing mortality from infectious diseases, no comparable improvements have occurred in the prevention of accidental poisonings.

While children are the most frequent victims, the fault of negligence does not necessarily rest at the doorstep of the parents, Conley added.

"Most of the children who take poison are active and curious," he said, "and most of the substances ingested by them are easily accessible. Even the parents failed to realize that a number of common household substances were poisonous until after the accident occurred. The model law will help parents become more aware of the hazards and thereby reduce fatalities."

► A copy of "Yugoslav Postage Stamps with Designs from the Fauna of the Adriatic Sea" may be obtained post-free on application to 'Jugofilatelija', Palmoticeva ul. 2, Beograd, Yugoslavia.

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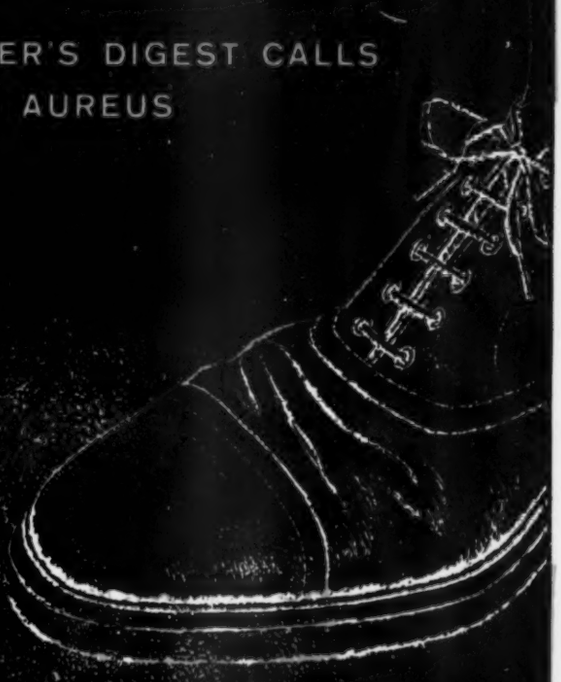

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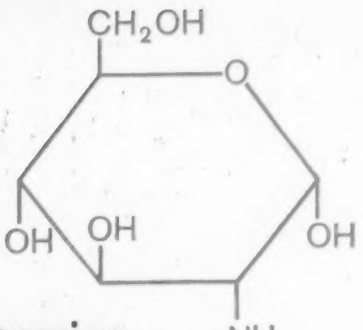

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Arizona Society

Members of the Arizona Society of Hospital Pharmacists met on January 19 at 2:00 P.M. at St. Mary's Hospital in Tucson. Routine reports were presented and Dr. Doris Hawkins discussed the work of the ASHP Committee on Safety Practices and Procedures.

The program included a report on the chemistry of steroids by Mr. Ken Kirkwood, a graduate of the University of Arizona; a discussion of electrolytic therapy by the Director of Laboratory Research at Cutter Laboratories; and a discussion of the poison control center which is being set up at the University of Arizona by Dr. Albert Picchioni.

The February meeting of the Arizona Society was scheduled for the 16th at St. Luke's Hospital in Phoenix.

Akron Area Society

Members of the Akron Area Society of Hospital Pharmacists heard Dr. William H. Voorheis speak on "Radio Biology" at the January 14 meeting. He discussed the fundamentals of radiation and offered an opportunity for discussion from the floor.

Business transacted at the January meeting of the Akron Area Society included the resignation of the Secretary, Mr. Samuel Arlow who has accepted a position in Cleveland. Mr. Charles R. Weiss, staff pharmacist at the Akron General Hospital, was named to fill the unexpired term of Mr. Arlow.

Plans were made for holding the Student Visitation Project in Akron on April 15 and 16. Other forthcoming events discussed included a visit to Parke, Davis and Co. and a Pfizer Seminar. An open discussion of general problems related to hospital pharmacy completed the business meeting.

Houston Area Society

The Houston Area Society installed as officers for 1958, Robert Lantos of Galveston, *President;* Tom Horner of Houston, *Vice-President;* and Adela Schneider of Houston, *Secretary-Treasurer.*

The installation meeting was held at the Southern Pacific Hospital in Houston on Sunday afternoon, January 26. Open House in the pharmacy, a short program on Prepaid Medical Care, and a Coffee Hour preceded the meeting at which John Freels, outgoing President, presided.

Robert Lantos was named delegate to the ASHP Convention, with Susan Campbell of Beaumont as alternate. The new President appointed the following committees: Program—Tom Horner and John Freels; and Membership—Adela Schneider, Dorothea Siler, and Henry Beard.

As a group project for the year the Society decided to give financial assistance from the chapter treasury to the Gulf Coast Poison Information Center from time to time during the year.

Northern California Society

The one hundred tenth meeting of the Northern California Society of Hospital Pharmacists was held on December 10 at the University of California Medical Center in San Francisco. The principal speaker was Dr. John W. Farquhar of the University of California who discussed "Factors That Control Serum Lipids and Their Role in Atherosclerosis."

The program also included an address by Mr. James McGoldrick, President of the Northern California Pharmaceutical Association who spoke on the activities of his organization and the State group as well as the newly organized Pharmaceutical Institute which is primarily concerned with legislation affecting pharmacy practice in California. Mr. McGoldrick urged all hospital pharmacists to join in a united effort to help promote the highest ethical standards for the profession.

Mr. William Eames of the Brookside General Hospital in San Pablo was introduced as a new active member of the Northern California Society.

The one hundred eleventh meeting of the Northern California Society of Hospital Pharmacists was held on January 14, 1958 at a dinner for installation of officers at the Villa De La Paix Restaurant in Oakland. Eighty members and guests attended the dinner, which was preceded by a Social Hour sponsored by Wyeth Laboratories.

Program Chairman Al Seubert introduced distinguished guests including Mrs. Marie B. Kuck, Dean and Mrs. Troy Daniels, Mr. Louis Fischl, and Mr. and Mrs. James McGoldrick. Helen and Barry Oliver, students at the University of California in Berkeley, entertained the group with folk songs. Francis Spinelli conducted a raffle of gifts donated by local pharmaceutical firms.

Out-going President Eric Owyang thanked the members of the Society for their cooperation during the past year and urged that all of Pharmacy strive for unity in attaining higher professional standards, and then turned the gavel over to Mathilde Herby, 1958 President.

Mrs. Herby introduced the following incoming officers: *Vice-President,* Jessie Lavender; *Secretary,* Molly Chin; and *Treasurer,* Charles Jackson. She set as one of her goals for 1958 a membership campaign to include all of Northern California and greater participation in activities of the Society by members in isolated areas.

Illinois Society

The Illinois Society of Hospital Pharmacists conducted its First Student Visitation Day Program on January 14. This was sponsored in cooperation with the Illinois Hospital Association, the Chicago Hospital Council and seven hospitals throughout the Chicago area. Invitations had been extended to members of the senior class of the University of Illinois and the class was divided into small groups each visiting a particular hospital. Each hospital visit included the following schedule:

A. Orientation by the Chief Pharmacist.
B. Touring of selected departments.
    1. Clinical Laboratories
    2. X-ray Department
    3. Operating Room
    4. Blood Bank
    5. Physical Therapy
    6. Maintenance Shop
    7. Boiler Room
    8. Purchases and Central Stores
    9. Central Service Department

10. Outpatient Department
11. Admitting Office
12. Emergency Room
13. Research Laboratories
14. Housekeeping Department
15. Pediatric Department
16. Recovery Room

C. Interviews with staff representatives of the following departments:
1. Administrative Staff
2. Medical Staff
3. Nursing Staff

D. Return to pharmacy and summary of tour.

5:30 P.M.

Dinner at the Hospital Restaurant

Those participating in the Student Visitation Project were also invited to attend a regular monthly meeting of the Illinois Society which was held at the U. S. Public Health Service Hospital at 8:00 P.M. Since the general theme for the year's programs is that of hospital problems affecting the pharmacy, the program for the January meeting was concerned with interdepartmental problems. A panel included Mr. Howard Cook, *Moderator*, Administrator, Community Hospital, along with the following panel members: Mr. Peter Solyom, Chief Pharmacist, University of Chicago Clinics; Miss May Werrbach, Nursing Supervisor, Chicago Wesley Memorial Hospital; Mr. Robert Berczon, Staff Representative, American Hospital Association; and Dr. Warren C. Jenkins, Community Hospital,

The Student Visitation Project was in charge of Mr. Edgar Duncan, Chairman, Mr. Joseph Oddis, Mr. James Palmgren, and Mr. Peter Solyom.

Philadelphia Hospital Pharmacists

The Philadelphia Hospital Pharmacists' Association is sponsoring a speaking program directed toward preventing accidental poisonings in homes. According to a message to community organizations from Mr. Herbert L. Flack, President of the Philadelphia Hospital Pharmacists' Association, the Association has a Speakers' Bureau which includes pharmacists in hospitals in the Greater Delaware Valley Area. The program is being offered as a public service to communities in the area and represents no commercial interests.

Michigan Society

Mr. Leo F. Godley, President of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, was the guest speaker at the January 16 meeting of the Michigan Society of Hospital Pharmacists. The meeting was held at the Veterans' Memorial Building in Detroit with Mr. Maxwell Miller presiding and Mr. Clifton Latiolais in charge of the Program. The hosts for the evening were representatives of E. R. Squibb and Son including Mr. John R. Kenny, Jr. who is with the Hospital Sales Department in New York City.

In Mr. Godley's presentation, he discussed in detail the work of the National Organization and plans which are developing for the future.

Business transacted during the meeting included a report from Mr. Clifton Latiolais, Chairman of the H.A.K. Whitney Award. Mr. Latiolais was selected as the delegate to attend the National Convention in Los Angeles in April as well as represent the Society in presenting the H.A.K. Whitney Award.

Colorado Society

The Colorado Society of Hospital Pharmacists sponsors a regular column in *The Rocky Mountain Druggist* which is edited by J. Conklin LaNier, II, Publicity Director for the Colorado Society. Mr. LaNier is Chief Pharmacist at the National Jewish Hospital in Denver and was formerly associated with the University of Chicago Clinics, Chicago, Illinois.

Midwest Sisters' Association

The February 20 meeting of the Midwest Association of Sister Pharmacists was held at the St. Bernard Hospital in Chicago. The program included papers on "The Artificial Kidney from the Pharmacist's Viewpoint," by Mr. J. Darst, Travenol Laboratories; "The Kidney and Its Part in the Conquest of Disease," also by Mr. J. Darst; and "The Kidney and Diets," by a dietitian from St. Bernard Hospital.

Northeastern New York Society

The Northeastern New York Society has recently published Number IV Volume I of *The Bulletin of the New York Society of Hospital Pharmacists*. In an editorial by President Louis P. Jeffrey, he urges all hospital pharmacists to participate in the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, as well as other organizations related to their professional activities. *The Bulletin*, published quarterly, appears in mimeographed form with contributions by various members of the organization. Articles of particular note appearing in Number IV include one on Pittsfield General Hospital, Pittsfield, Mass., by Marco Gasbarrone; Anticonvulsant Drugs by Benjamin Teplitsky; A Method of Control in Hospital Pharmacy, by Fay Peck, Jr.; and Hospital Pharmacist of the Month—Lucy M. Manvel, by Violet S. Spaulding.

Greater Kansas City Society

The Society of Hospital Pharmacists of Greater Kansas City met at the Blue Cross-Blue Shield Building on Wednesday, December 11 with President Charles Loomis presiding. Fifteen members were present. Business included a report on Civil Defense by Mr. Loomis along with routine reports. The group also decided to study Article VI of the Minimum Standard for Pharmacies in Hospitals as part of the request from the ASHP Committee on Special Projects.

Officers for the year were elected including J. C. Chipman, *President;* Frank Huff, *Vice-President*; Sister Rose Bernard, *Secretary;* and Sister Mary Andrew, *Treasurer.*

Southern California Society

The annual installation dinner meeting of the Southern California Society of Hospital Pharmacists was held January 8, 1958, to honor the newly elected officers. Cecil Stewart, Executive Secretary of the California Pharmaceutical Association, was the speaker of the evening. His topic stressed the importance of all the Society members affiliating with the organization, pointing out that by joining together as a team, professional pharmacy can better assert itself to take its rightful place in the medical profession.

Joseph H. Beckerman, Assistant Chief Pharmacist at the University of California Hospital at Los Angeles, was installed as *President.* Serving with Mr. Beckerman are: Dr. John H. Plake, White Memorial Hospital, *Vice-President;* Wendell Hill, Orange County Hospital, *Treasurer;* and Ethel B. Kopple, Crenshaw Hospital, as *Recording Secretary.*

More than 100 members and guests attended this annual event, and from the apparent enthusiasm, a most successful year is anticipated.

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1. Hunter, J.A., et al.: Hospital Management *83*:86 (March) 1957.

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Louisiana Society

Dr. R. W. Sappenfield, Pediatrician on the staff of the Louisiana State University Medical School, spoke to the Louisiana Society of Hospital Pharmacists at a meeting on January 16, 1958 held at Charity Hospital. The topic discussed concerned the movement to establish a Poison Control Center in New Orleans. Dr. Sappenfield traced the history of the movement throughout the country and its status in Louisiana. Dr. Sappenfield pointed out that the cooperation of pharmacists in Louisiana is sought in connection with this project and that an advisory committee, to be formed soon, would include a representative of the Society.

The annual meeting of the Society was discussed and a tentative agenda was presented. The meeting is to take place on March 21st in Baton Rouge, La. Mr. Albert Lauve will write to Mr. Leo Godley to ask if he will address the Louisiana Society at this meeting.

Mercy Hospital in New Orleans, La. was the recipient of a Poison Emergency Cabinet donated by the L.S.H.P. under a judgment initiated jointly with the L.S.P.A.

Oklahoma Society

More than thirty hospital pharmacists were present for the first 1958 meeting held at the Auditorium of St. Anthony Hospital Nurses Residence on January 16. The meeting was opened by Mr. Ralph E. Reed, President.

The guest speaker for the evening was Dr. Harold Shoemaker, of the Department of Pharmacology of the Oklahoma University Medical School. Dr. Shoemaker spoke at length on General Toxicology, and informed those present of the Poison Information Center in Oklahoma City. This Center is connected with the University Hospital, someone is on call twenty four hours a day, and on days when the personnel is not on duty, he (Dr. Shoemaker) will take the calls himself. He informed us also that the file for information on poisons and treatments contains about 30,000 cards with the needed information. He presented a number of cases who have been treated as the result of the information so readily available at the center.

During the business meeting President Reed appointed the following committee members for the coming year:

Program: A. E. Biggs, *Chairman,* U.S.P.H.S. Hospital for Indians, Lawton; Mrs. Mayme Shillings, Wesley Hospital, Oklahoma City; Mr. Stokes E. Baggett, V. A. Hospital, Oklahoma City; Miss Frances Heaney, Hillcrest Memorial, Tulsa; and Mr. Dan Clemons, Valley View Hospital, Ada, Okla.

Constitution and By-Laws: Mr. Joe R. Davis, *Chairman,* V.A. Hospital, Oklahoma City; Mr. George L. West, University Hospitals, Oklahoma City; Miss Marguerite Jones, Hillcrest Memorial, Tulsa; Mr. David McLemore, Oklahoma City; and Miss Addie L. Weaver, Miami, Oklahoma.

Resolutions: Mr. Charles Freeman, *Chairman,* Wesley Hospital; Miss Wanda Lee Teakell, St. Anthony Hospital; and Mrs. Betty Powers Perdue, Mercy Hospital, all of Oklahoma City.

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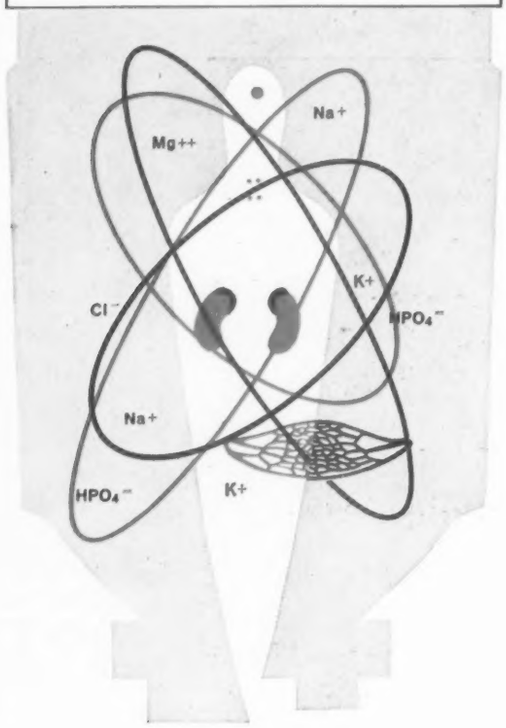

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*Combined results of 12 independent clinical investigators. Data available on request.

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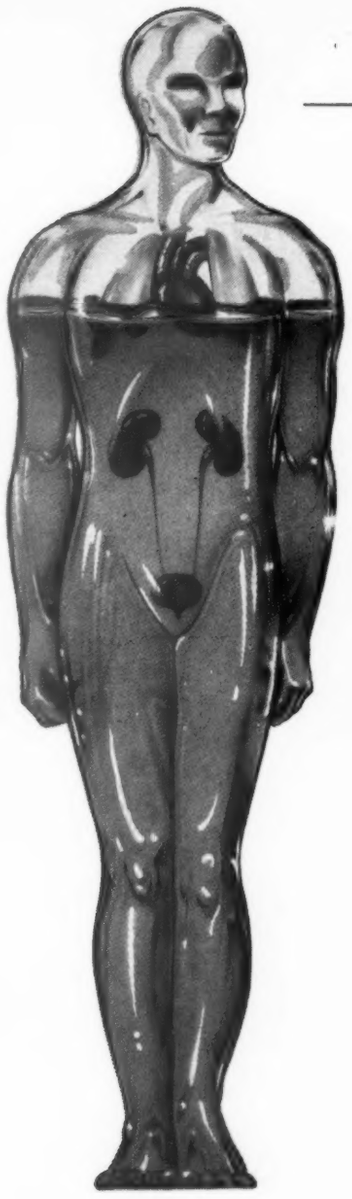

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REFERENCES: Baer, J. E. *et al.:* Fed. Proc. **16**:278 (March) 1957; Beyer, K. H. *et al.:* Fed. Proc. **16**:282 (March) 1957; Ford, R. V. *et al.:* M. Rec. & Ann. **51**:376 (April) 1957; Ford, R. V. *et al.:* Arch. Int. Med. **100**:582 (Oct.) 1957; Ford, R. V. *et al.:* Antibiotic Med. & Clin. Therapy (in press); Moyer, J. H. *et al.:* Proc. Soc. Exper. Biol. & Med. (in press); Novello, F. C. and Sprague, J. M.: J. Am. Chem. Soc. **79**:2028 (April 20) 1957; Russo, H. F. *et al.:* Fed. Proc. **16**:333 (March) 1957.

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REFERENCES: Hollander, W. and Wilkins, R. W.: Boston Med. Quart. **8**:69 (Sept.) 1957; Freis, E. D. *et al.:* J.A.M.A. (in press); Finnerty, F. A.: N. Y. State J. Med. **57**:2957 (Sept. 15) 1957; Freis, E. D. and Wilson, I. M.: Med. Ann. District of Columbia **26**:468 (Sept.) 1957; Freis, E. D. *et al:* Circulation (in press).

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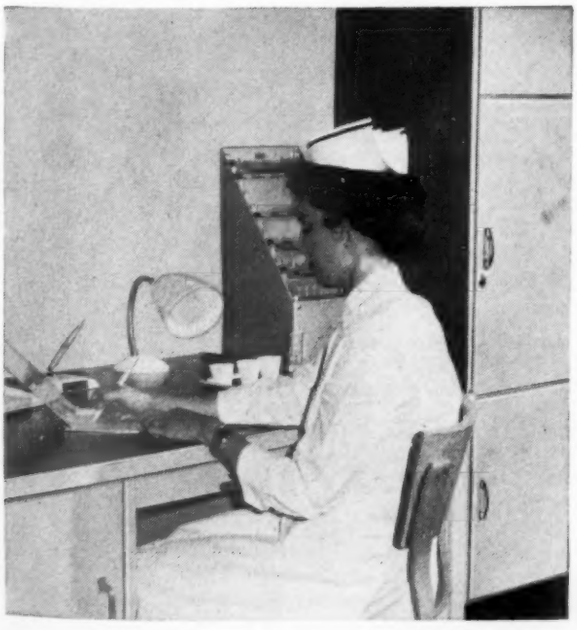

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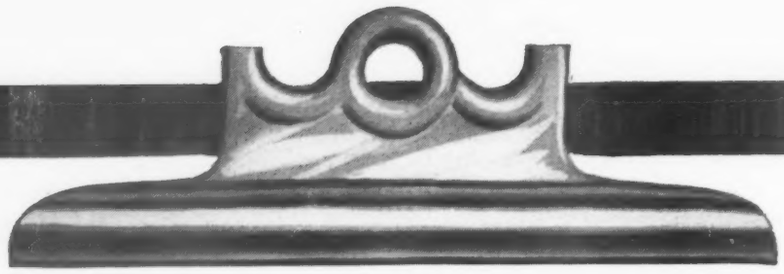

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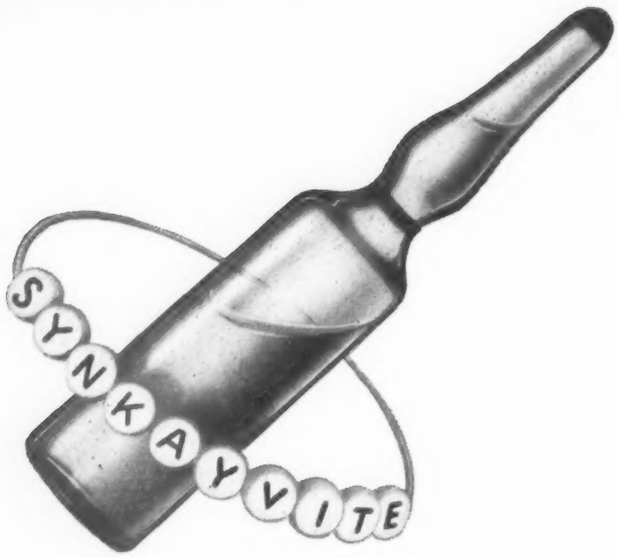
References: 1. Altschul, A. and Billow, B.: The clinical use of meprobamate (Miltown®). New York J. Med. 57:2361, July 15, 1957. 2. Atwater, J. S.: The use of anticholinergic agents in peptic ulcer therapy. J. M. A. Georgia 45:421, Oct. 1956. 3. Borrus, J. C.: Study of effect of Miltown (2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate) on psychiatric states. J. A. M. A. 157:1596, April 30, 1955. 4. Cayer, D.: Prolonged anticholinergic therapy of duodenal ulcer. Am. J. Digest. Dis. 1:301, July 1956. 5. Marquis, D. G. Kelly, E. L., Miller, J. G., Gerard, R. W., and Rapoport, A.: Experimental studies of behavioral effects of meprobamate on normal subjects. Ann. New York Acad. Sc. 67:701, May 9, 1957. 6. Phillips, R. E.: Use of meprobamate (Miltown®) for the treatment of emotional disorders. Am. Pract. & Digest Treat. 7:1573, Oct. 1956. 7. Selling, L. S.: A clinical study of Miltown®, a new tranquilizing agent. J. Clin. & Exper. Psychopath. 17:7, March 1956. 8. Wolf, S. and Wolff, H. G.: Human Gastric Function, Oxford University Press, New York, 1947.



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Alvin Hansen of Harvard University is quoted on the subject: "The conflict . . . between a rigidly private-enterprise point of view and a social-welfare point of view."

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LUDWIG PESA
Chief Pharmacist

St. Mary's Hospital
Passaic, New Jersey

Appreciation

DEAR SIRS: I wish to take this opportunity of complimenting the editorial staff of the AMERICAN JOURNAL OF HOSPITAL PHARMACY for an excellent publication. The exchange of information this journal affords plays an indispensable part in the advancement of our profession.

NEAL SCHWARTAU
Chief Pharmacist

Rochester Methodist Hospital
Rochester, Minnesota

DEAR SIRS: May I enthusiastically extend my personal congratulations on the appearance and text of the first issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. All of the trials and tribulations suffered by the editors in surviving the fourteen volumes of *The Bulletin* represent past history but only on such a past can a bright, informative publication be built. I am certain that the new JOURNAL will continue the policy of leading hospital pharmacists towards improved service to their communities by means of scientific articles of high calibre and constant editorial prodding. The JOURNAL has under its previous name endeavored to elevate the profession of pharmacy by supporting an exchange of ideas and opinions between hospital pharmacists, pharmaceutical educators, and industrial pharmacists and will in its new format undoubtedly continue support of such collaboration.

The AMERICAN SOCIETY OF HOSPITAL PHARMACISTS deserves the applause of all pharmacists for their support in developing such a fine publication. With best wishes for a long and happy career in the family of scientific publications.

JACK COOPER, *Director*
Pharmacy Research and Development Division
Ciba Pharmaceutical Products Inc.
Summit, New Jersey

DEAR SIRS: THE FRESH NEW APPEARANCE AND NAME OF OUR OFFICIAL PUBLICATION IS SPLENDID. WE ARE ALL HAPPY TO HEAR THAT IT WILL BE PUBLISHED MONTHLY. THE NEW DEPARTMENTS ARE FINE, ESPECIALLY "CONSULTING WITH BOWLES." CONGRATULATIONS.

SISTER M. GONZALES
Chief Pharmacist

Mercy Hospital
Pittsburgh, Pa.

DEAR SIRS: Congratulations on the new format of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. The "distinguished look" is most becoming.

BERNARD E. CONLEY, PH.D.
Secretary

Committee on Toxicology
American Medical Association
Chicago, Ill.

Correction

DEAR SIRS: I would like to call your attention to an incorrect listing of the Hospital Pharmacy Institutes for the year 1958 which appeared in the January issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. Although the dates are correct, the locations should be reversed. The correct listing should read:

1. Temple University, Philadelphia, Pennsylvania, June 16-20.

2. University of Chicago, Chicago, Illinois, July 28-August 1.

JOSEPH A. ODDIS, *Staff Representative*
Council on Professional Practice
American Hospital Association
Chicago 10, Illinois

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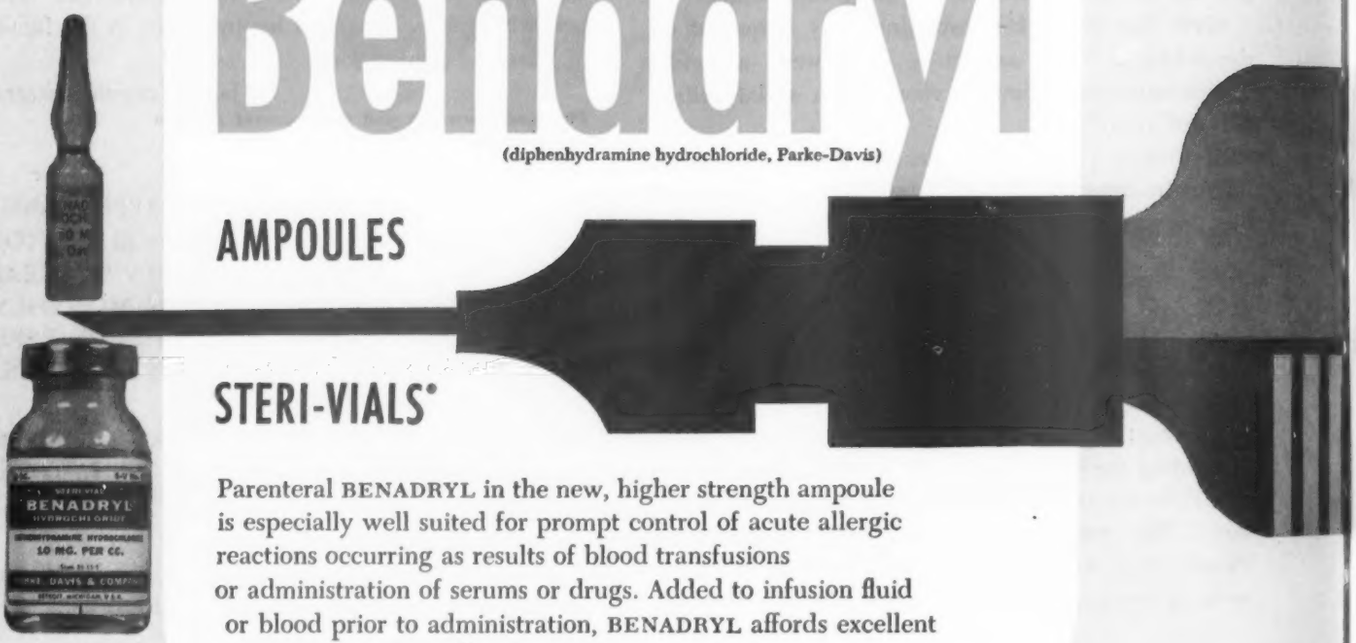

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editorial

by DON E. FRANCKE

A Student-Exchange Program For Pharmacists

► THE EXECUTIVE COMMITTEE OF THE ASHP recently voted to sponsor a program to promote the exchange of pharmacy students and recent graduates between foreign countries and the United States. Objectives of the program are to allow American students to visit other countries and to allow foreign students to visit the United States to gain diversified experience in hospital pharmacy and to obtain a knowledge of the cultural and pharmaceutical life of the countries visited.

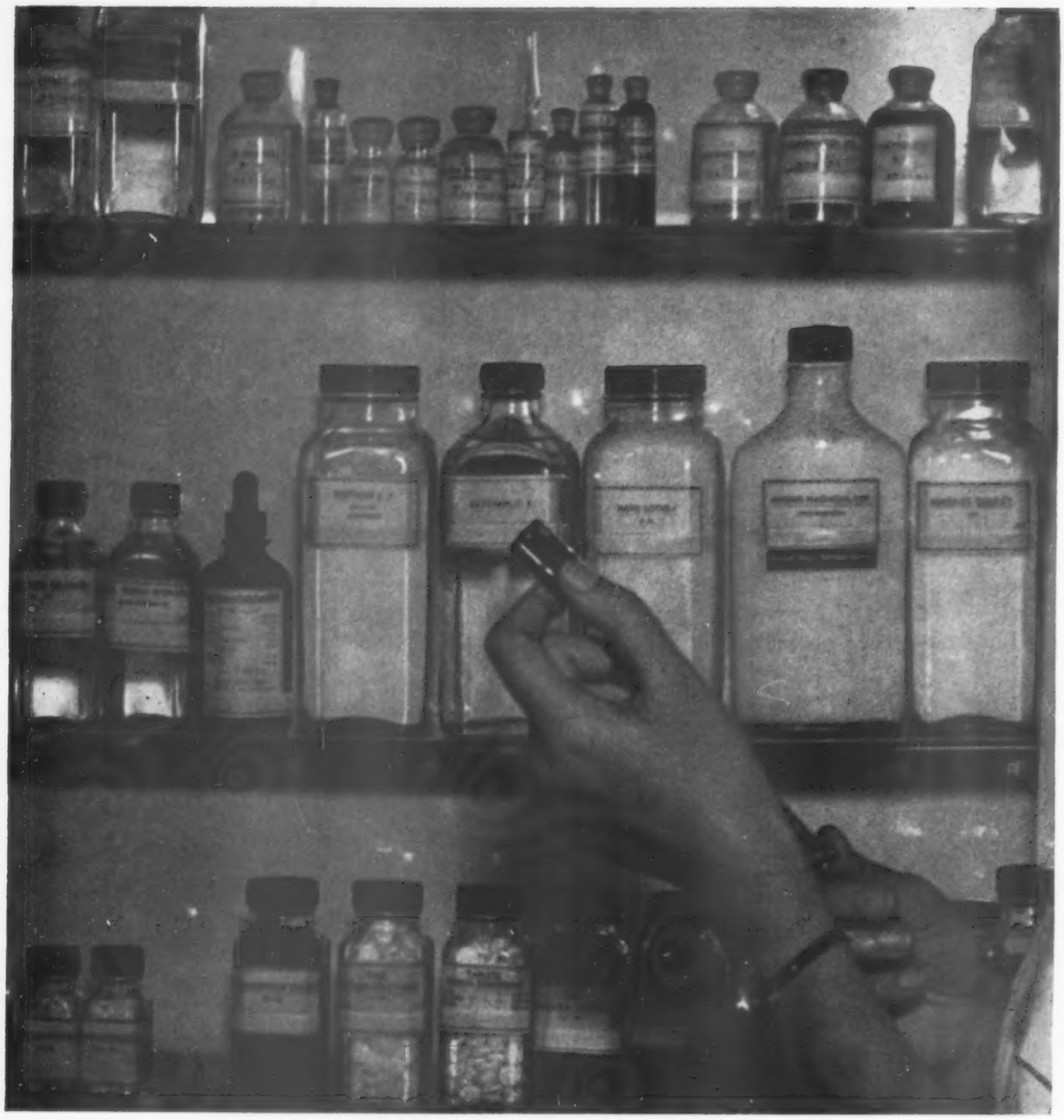
While the ASHP Executive Committee has voted to sponsor the student-exchange program, official approval of the U. S. State Department must be obtained before the program can be implemented.

At present there is no national pharmaceutical organization in the United States which participates on a formal basis in the student-exchange program of the International Pharmaceutical Students' Federation. It has been suggested that an ideal arrangement would be one in which the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS sponsored a program for hospital pharmacists and the American College of Apothecaries sponsored a similar program for retail pharmacists.

The SOCIETY'S program would be operated in cooperation with the student-exchange program of the International Pharmaceutical Students' Federation. The latter, an affiliate of the Fédération Internationale Pharmaceutique, is composed of students from 24 countries, including the United States. The Students' Federation has been active for several years in fostering student-exchange programs and more than 130 individual exchanges have been arranged during the past two years. The Students' Federation has an American Liaison Secretary, Dr. Jerome Reinstein of the School of Pharmacy at the University of Wisconsin, who has offered to cooperate with the SOCIETY in this venture. He would receive applications from American students who wish to be assigned to European pharmacies and transmit them to the Chairman of the I.P.S.F. Student-Exchange program, Dr. H. van der Meer of Leiden, Holland. In addition, Dr. Reinstein would receive from Dr. van der Meer applications from European students who wish to be assigned to hospital pharmacies in America. These applications would, in turn, be transmitted to the SOCIETY so that the applicants might be placed in hospital pharmacies cooperating in the program.

The general plan of the student-exchange program would be somewhat as follows. Pharmacy students or recent graduates would make application, specifying the country in which they would like to receive experience. The student may apply to work or to observe in a hospital pharmacy. The host pharmacist may accept a student for work or observation, whichever plan is mutually acceptable. The exchange period may be from one to three months, usually during the summer vacation period. Students pay their own transportation expenses. All students participating in the exchange program must be covered by health and accident insurance. Insurance may be obtained from the I.P.S.F. or from other sources. The student should receive from the hospital free board and lodging and a small amount of spending money, or a stipend sufficient to pay these expenses.

Successful implementation of the student-exchange program will provide American pharmacy students and recent graduates an opportunity to observe hospital pharmacy and retail pharmacy as they are practiced in other countries. While doing this, they may also observe the status of the European pharmacist in society and his role in public health activities; they may perfect their speaking and reading knowledge of a foreign language; they may take advantage of numerous cultural opportunities which will present themselves; and they may promote a greater mutual understanding between the pharmacists of the United States and other countries. Such a program would be a rich experience for American pharmacists whether they intend to enter hospital or retail practice.



qualifications and responsibilities of

LAY HELP

in the

hospital pharmacy

by GEORGE F. ARCHAMBAULT

► I HAVE BEEN REQUESTED to discuss with you the qualifications and responsibilities of lay help in the pharmacies of the nation's hospitals.

GEORGE F. ARCHAMBAULT, Ph.C., D.Sc., LL.B., is Chief, Pharmacy Branch, Division of Hospitals, U.S. Public Health Service, Department of Health, Education, and Welfare, Washington, D. C.

Presented April, 1957, Annual Meeting, AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, New York City, New York.

Let me start by mentioning *not* what tragedies might occur when this important matter in hospital administration is neglected, but rather by presenting some of the tragedies that have actually occurred in hospitals where lay help have been allowed to handle medications in the pharmacy without direct supervision by the pharmacist.

Within recent years, non-pharmacists in dispensing medications in hospitals, have been involved in the deaths of infants in a hospital nursery as a result of the issuance of a boric acid solution for one of glucose and the death of two adults by dispensing sodium nitrite for sodium phosphate.

Acts of Carelessness

Concerning the two deaths involving sodium nitrite, the Presiding Justice of the District Court in the city involved had the following to say in his Inquest report —"Suffice to say, however, a study of the evidence reveals acts of carelessness, carefree abandonment of responsibilities, the delegation of responsibilities to others, certain omissions to act, and wanton and reckless acts, as well as incompetence and the failure to qualify for the jobs they were intended to do on the part of the Director of the————————Hospital; the Chief Pharmacist of the————————Hospital and the *pharmacist helper* so as to warrant and justify a finding of criminal negligence on the part of the above named and described individuals, and by reason thereof, that is the finding of the courts."

The Grand Jury on hearing the case, while not naming individuals, indicted the hospital on a lesser charge than criminal negligence—a charge of violating a State Public Health Department regulation. At trial in criminal court, the hospital was convicted of the charge and received the maximum fine—$500.

Blind Spot in Administration

A check of the August 1956 Administrative Guide Issue of *Hospitals,* the Journal of The American Hospital Association, reveals some rather astounding facts. Of the 5,237 short-term hospitals in continental United States, some 2,309 reported no pharmacies and 3,683 reported that they do not have a pharmacist in their employ. This is a serious "blind spot" in hospital administration. It would appear that some hospital administrators are allowing or fostering the improper utilization of nonprofessional personnel in this dangerous area of drug issuance; a utilization that is in direct violation of the Pharmacy and Hospital Licensing Acts of many States and contrary to the pharmacy elements of the Joint Commission on the Accreditation of Hospitals.

Some Serious Problems

Hospital administrators and hospital pharmacists must now give serious thought to the proper solutions of the problems of (1) no pharmacist supervision over drugs in many of the small hospitals of the nation, (2) too few pharmacists in some of the larger hospitals where pharmacy helpers are performing the work of pharmacists, without supervision, and with the expressed or implied consent of the pharmacist and/or administrator, (3) the policy employed by some hospitals of permitting ward attendants and others, including nurses to enter the pharmacy and dispense medications in the absence of the pharmacist, (4) the liability of the hospital in criminal and tort negligence suits arising from injuries or deaths where a nonprofessional helper, a non-pharmacist, acts as a licensed pharmacist with the consent of the hospital, (5) the personal liability of the trustees, the administrator, and the pharmacist in these situations and (6) the proper utilization of nonprofessionals in the pharmacy department.

Now let us spend a few minutes discussing the problem of proper utilization of nonprofessionals in the pharmacy department.

Dangerous Waters

Let us bring this problem of proper utilization of non-pharmacists in hospital pharmacies close to home —to be specific, to *your* pharmacy and to mine. Do we, in collusion with our administrator or worse still, without his knowledge, allow nonprofessionals (pharmacy helpers and others), to engage in duties that we know the law of our state demands be performed only by licensed pharmacists? I refer in particular to certain acts of compounding and dispensing and the filling of nursing station medication containers where no immediate, direct pharmacist supervision is exercised. If we do, we are treading in dangerous waters.

Last year at the Harvey A. K. Whitney Lecture, I spoke on *Ethical Standards for Hospital Pharmacists.** Let me quote a paragraph from that presentation.

> We hospital pharmacists, unlike our esteemed colleagues of the pharmaceutical profession who practice as private individuals, as the community practitioners of pharmacy, serve in institutions as public employees. As such, we are subject to supervision and direction which normally constitutes restraints on unethical conduct not present in the case of the community practitioner of pharmacy. Like the hospital-employed physician, dentist, and nurse, the hospital pharmacist recognizes that administration may state 'where' and 'when' to practice but never 'how' to practice. This is an important concept that must not be lost sight of. In the final analysis, this 'how' is the practice of pharmacy (in all

* Bull. Am. Soc. Hosp. Pharm. 13:444 (Sept.-Oct.) 1956

POSITION DESCRIPTION OF PHARMACY HELPER-STOREKEEPER

Description of Duties and Responsibilities

Under the *direct* and *immediate* supervision of a pharmacist, performs subordinate work, including the bulk compounding of simple *external* use pharmaceutical preparations. This work is subject to ingredient check, weighing and measuring checks, and final inspection of the pharmacist. Assists the pharmacist in filling prescriptions and requisitions, in bulk compounding and prepackaging. Is responsible for maintenance of stock control of drugs and prepares reports and performs other duties as may be required incident to the general care and operation of the pharmacy.

Duties and Major Steps Taken to Perform Duties

I. PHARMACEUTICAL DUTIES—Assists pharmacist in:

1. Compounding *external use* preparations:
   a. Ointments in 15 pound lots in electric mixer;
   b. Ointments in small quantities on slab or in mortar or ointment mill;
   c. Solutions in 30 gallon lots by means of electric mixer, and filter through electric filter;
   d. Solutions, rubbing alcohol, lotions and sprays in gallon or 5 gallon lots, with aid of electric mixer or by hand;
   e. Mix powders by means of Blender (electric) or by hand in mortar;
   f. Homogenize creams and lotions in electric homogenizer;
   g. Also fills capsules of various sizes with powdered drugs by machine or by hand:
2. Filling prescriptions for patients:
3. Prepackaging, labeling and affixing control numbers to drugs for dispensing:
4. Collecting containers from various departments, such as nursing station medication centers, filling them from stock preparations previously made in compounding department, and delivering them to the proper department;
5. Maintaining pharmaceutical records:
   a. Pharmaceutical bulk compounding worksheet;
   b. Pharmaceutical formulation control record;
   c. Prepackaged pharmaceutical item control record;
   d. Chronological log for bulk compounded items;
   e. Others.

II. PHARMACY STOCK CONTROL DUTIES

1. Maintain stock control Kardex system:
   a. Purchase order information posted when order is placed;
   b. Receiving report information posted when order is received, drugs are checked against purchase order and receiving report;
   c. Each drug item is dated and stored in proper section of storeroom;
   d. New cards and inserts are typed as indicated;
   e. Signal is moved back to "Normal" position of title insert;
   f. When drugs are issued, information and balance is posted and Kardex record adjusted;
   g. Unit prices are entered, extensions and adjustments in unit prices are made, as indicated;
   h. Issues are entered weekly (or more often) on Storeroom Request and Issue Record Forms for use of cost accounting section;
   i. Kardex is reconciled monthly with cost accounting section;
   j. A physical inventory is taken quarterly for reconciliation purposes;
   k. Cards are ruled monthly and inventory balance entered beneath ruled line;
   l. Issues are totaled and entered on "Experience" card at end of month;
   m. Experience card is totaled yearly for administrative use;
   n. Approximately 850 drugs are carried as stock items on Kardex.
2. Maintain Drug Storeroom:
   a. Clean bottles of excelsior and dust before placing on shelf;
   b. Arrange stock in alphabetical order;
   c. See that "shelf stripping" is kept clean and up-to-date and correct stock number listed:
   d. Place new stock behind old to insure proper utilization;
   e. Rearrange stock as necessary after each issue;
   f. Dust storeroom shelves weekly.

III. MISCELLANEOUS DUTIES

1. Perform or supervise general cleaning and dusting of pharmacy areas:
2. Clean glassware and other pharmaceutical equipment:
3. Wash bottles, change labels on stock bottles, renew labels and apply label protective:

Performance Requirements

I. PHARMACEUTICAL DUTIES

1. Employee is expected to be sufficiently skilled in compounding external use pharmaceutical preparations by means of electrical equipment and by hand, so that products are quickly and properly made. Must lift and carry cartons and drug orders which may be fairly heavy. Is expected to be accurate in performing assigned duties; must be willing to perform routine, repetitive tasks on a continuous basis. Must be cooperative with others and able to take orders readily and follow directions precisely.
2. Works under *direct and immediate supervision;* receives explicit instructions and supervision while tasks are new; supervision lessens as worker gains experience, *but always under general supervision and checked on each pharmaceutical process handled.* Must maintain proper professional decorum in the pharmacy.
3. Must use proper technique in pouring from stock bottles, in counting pills, tablets and capsules, using tablet "counter" to avoid contact of the medication with the hands. Must be prompt and accurate in delivering supplies to each department.
4. Records must be executed at time of compounding in order to have a correct check of ingredients used. Must spell correctly; write neatly and make accurate calculations.

II. PHARMACY STOCK CONTROL DUTIES

1. Supply clerk is expected to be skilled in handling Kardex system according to regulations in stock Control Manual, in that he is under general supervision only. The objective of stock control is to provide at all times an adequate supply of drugs. This is accomplished by keeping current a complete record of all purchases, receipts, issues and balances. He must maintain perpetual inventory figures, periodically verified by actual physical inventories. At end of each month, Kardex records must be completed in order to provide figures for monthly Pharmacy Operations Report.
2. The drug stock must be kept in alphabetical arrangement; "shelf stripping" must be kept in order so that each item is stored in proper section. The stock must check with balance shown on Kardex (perpetual inventory) at all times; it must be ready for "spot" inspection at any time.

III. MISCELLANEOUS DUTIES

1. Is expected to supervise or handle the cleaning of all pharmacy areas; wash bottles and glassware; must know what cleaning compounds to use to remove drug residues after compounding.

Knowledge, Skills and Abilities Used

I. PHARMACEUTICAL DUTIES

1. Knowledge of physical properties of drugs used in preparations compounded with their trade, synonym and generic names, in order to check for deterioration or error; drug solubilities in order to facilitate bulk compounding of external preparations; scales and balances; weights and measures (metric and apothecary) and how to convert from one system to the other, and simple pharmaceutical calculations. Should have skill in manipulating balances, care of still, mixers, homogenizer, filter, and hand tube filling apparatus. Skill is experience acquired as a Junior Pharmacy Helper or otherwise in fulfilling pharmaceutical duties in a professional manner; skill is exercised in pouring from stock bottles to prevent label spoilage. Mental ability to perform mathematical calculations accurately and promptly is essential, also physical ability to handle cartons and drug orders of a bulky nature.
2. Knowledge of prescription form; ability to read prescriptions and signas; to type labels and affix to containers correctly and neatly.
3. Ability to deal intelligently and courteously with various department heads.
4. Skill in preparing neat, properly labeled packages or containers.
5. Knowledge of pharmaceutical formulas and forms; ability to write legibly and neatly; ability to file records and to wrap and package neatly.

II. PHARMACEUTICAL STOCK CONTROL DUTIES

1. Knowledge of Stock Control Manual. Knowledge of typewriter, calculating machine, Kardex assembly. Knowledge of arithmetic, filing, posting, generic, official synonym, and trade names of drugs in order to place in proper alphabetical arrangement the forms used for stock control records. Skill in handling necessary equipment, typewriter, calculating machine, Kardex assembly; skill in writing legibly and neatly in order to keep Kardex (perpetual inventory) properly. Mental ability required to make necessary mathematical calculations and price adjustments; to spell difficult names of drugs correctly.
2. Physical ability to handle large drums or cartons when receiving stock; opening large cartons; climbing ladder to store and clean stock on upper shelves.

III. MISCELLANEOUS DUTIES

1. Ability to direct janitors in cleaning floors, windows; waxing and polishing floors; dusting. Knowledge of cleaning compounds and skill in applying them. Ability to do manual labor incident to maintaining a clean pharmacy and storeroom.

of its ramifications, including *when* and *how* to use pharmacy helpers) for which the State has licensed the individual, not the hospital, not the administrator, nor the Board of Governors or trustees. The hospital pharmacist must stand alone before his peers, be it a Practice or Grievance or Ethical Standards Committee or a State Board of Pharmacy (or a court), for any unethical (or illegal act) or questionable professional practice, regardless by whom suggested or ordered. Let us not misunderstand this position and responsibility. An employee (the hospital) has the right to control the activities of the staff member (hospital pharmacist), the 'when' and 'where' of practice. However, the hospital pharmacist is responsible professionally, morally and legally for his own acts.

Apply this thinking, if you will, to your personal situation relative to the utilization of pharmacy helpers under your supervision and also to the method whereby drugs are issued from your pharmacy in the 'off' pharmacist hours. Are your patients safe? Are you safe from personal law suit? Is your hospital protected?

W.H.O. on Auxiliary Personnel

The expert Committe on Professional and Technical Education of Medical and Auxiliary Personnel of the World Health Organization in its third report (Technical Report Series 109) has this to say on this subject:

3.8 Auxiliaries for Pharmacists

In a number of countries, it has been found that auxiliary personnel can assist, or to some extent replace the fully qualified pharmacist. There are, of course, *potential risks* of drug mishandling and individual health administrations might prefer to limit the duties of such auxiliaries to the dispensing of drugs or medicines in *unbroken sealed containers,* which have themselves been produced by manufacturers or fully qualified pharmacists in official central or regional medical stores. In addition, special care must be taken in the assignment of duties involving dangerous drugs and drugs controlled by National and International Regulations.

Proper Utilization

I would like next to highlight briefly three points relative to the utilization of nonprofessionals in hospital pharmacies: (1) the method of their selection, (2) the desirable prerequisites for such individuals and (3) the nature of their duties and their responsibilities. Considerable thought has been given to these areas by personnel management leaders these past few years. Let me pass on to you some of their thinking in these areas.

Selection of Personnel

Before citing an acceptable technique in this area, let us remind ourselves of the reasons why pharmacy helpers are employed. They are employed to handle housekeeping, to aid in bulk compounding and prepackaging and in some situations to serve as storekeeper—that is to keep drug stores (inventory), to handle "shelf stripping" and to maintain perpetual inventory records. They are utilized also to collect and deliver nursing station medication baskets, to do stock checking, to handle storeroom arrangement, to keep perpetual inventory records, to dust and clean and to render assistance in prepackaging and bulk compounding (under close supervision). Obviously, the utilization of an aged ward attendant or other hospital employee as a pharmacy helper during his last 3 to 5 years of employment before retirement, is not a satisfactory solution to this problem. And yet, how often do we note the kind hearted administrator, seeking an easier job for a faithful aged employee, attempting to place such an employee in the pharmacy, forgetting for the moment the obligation to patients and the hospital?

Sound personnel practice requires that the personnel office do the recruiting for specific vacancies in the hospital. The personnel office screens applicants who obviously do not meet the requirements demanded of the position. Good personnel practice requires, when the labor market permits, the referring of no less than three qualified applicants to the Chief Pharmacist for interview, discussion of work, and final selection. In referring the applicant, it is the responsibility of the personnel office to make any pertinent recommendations indicated to guide the pharmacist in his selection. The Chief Pharmacist should make final selection based on such important factors as ability of the candidate to work with the pharmacy staff and his degree of efficiency.

Educational Prerequisites of Pharmacy Helpers

For sound personnel practice, two classes of positions are needed in this category—the trainee position which is that of a Junior Pharmacy Helper and the position of the trained individual.

Let us consider first the *characteristic* of the trainee position. Typically incumbents of positions in this class are acquiring on-the-job knowledge and skill in the performance of the duties of the Senior or trained lay individual in this class of work. The individual performs under the *very* close supervision of a pharmacist. The pharmacist is responsible for giving detailed and specific instructions and on-the-job training regarding the duties to be performed and the specific manner in which those tasks are to be carried out. The pharmacist is also responsible for closely observing performance of the work to insure accuracy.

Knowledge and Abilities of Applicants

Applicants for the trainee position of Pharmacy Helper must have the ability to acquire skill in the

use of the more ordinary pharmaceutical apparatus, instruments, and equipment, a knowledge of simple mathematics, the ability to follow simple oral or written instructions; carefulness in carrying out assignments; and exhibit evidence of such traits as neatness and cleanliness, manual dexterity, reliability and willingness to perform any manual task desired.

Now let us discuss the position of *Senior* Pharmacy Helper, often referred to as the Pharmacy Helper-Storekeeper position.

Positions in this class are those of *trained* Pharmacy Helpers assisting pharmacists in the simpler mixing techniques and those activities requiring considerable physical work. Also, such individuals may well have responsibility for stock control under general supervision only. Again, the work is performed under the supervision of a pharmacist who gives specific instructions regarding the duties to be performed and who reviews performance of the work at certain steps and checks the finished product.

Guidelines of work consist of practices, procedures, techniques and formulas as outlined by the supervisor pharmacist.

Incumbents of positions in this class, as a substantial duty, prepare a limited variety of routine stock solutions, ointments, creams and other preparations in accordance with specific instruction. Typically, they prepare bulk lots of such preparations as Dobell's solution, antiseptic solution, boric acid solution, camphor and soap liniment, rubbing alcohol and rubbing lotions. They mix ointments in large amounts and perform all the various operations involved, *i.e.* triturating the medicinal powder and sifting through the proper size sieve, placing the ointment base in the mixer either in solid or melted form, and levigating the ointment for the required period of time. They also package, under close review of a pharmacist, stock solutions, tablets, capsules and other items in various convenient size containers, affix labels thereon, and place them in their proper location on the shelves. This operation consists of taking a solution, ointment, powder or other preparation from large stock containers and filling smaller containers to facilitate dispensing of simple and routine preparations.

The trained pharmacy helper also aids in preparing the list of items to be requisitioned, receives incoming shipments of drugs and checks items received against shipping records and requisitions and notes shortages or breakage. He enters all incoming shipments of drugs on stock record cards; periodically assists with physical inventory of ward, clinic and operating room drug cabinets; cleans bottles, jars, vials or other containers and equipment and assists with maintaining drug cost records.

Knowledge, Abilities and Other Qualities

The *trained* helper moving into this position from the trainee position is expected to have skill in the use of the more ordinary pharmaceutical apparatus, instruments and equipment; good knowledge of the simpler pharmacy methods and techniques; a knowledge of simple mathematics; manual dexterity; ability to follow oral or written instructions, and reliability and carefulness in carrying out assignments.*

It is important to note in this entire discussion of qualifications and responsibilities of nonprofessionals in the pharmacy that the professional type work is performed under the *direct and immediate supervision* of a pharmacist and does not permit any deviation from the specific instructions given. Stock control and store keeper duties, however, while performed under supervision, require supervision of the general and not direct and immediate type.

I have attempted in this paper to cover the four major elements in considering the qualifications and responsibilities of the lay helper in hospital pharmacy.

A. The dangers inherent in the misuse of such personnel
B. A methodology in selecting pharmacy helpers
C. Educational prerequisites of such help for both the trainee and experienced helper, and
D. A summary of the responsibilities and duties inherent in these positions.

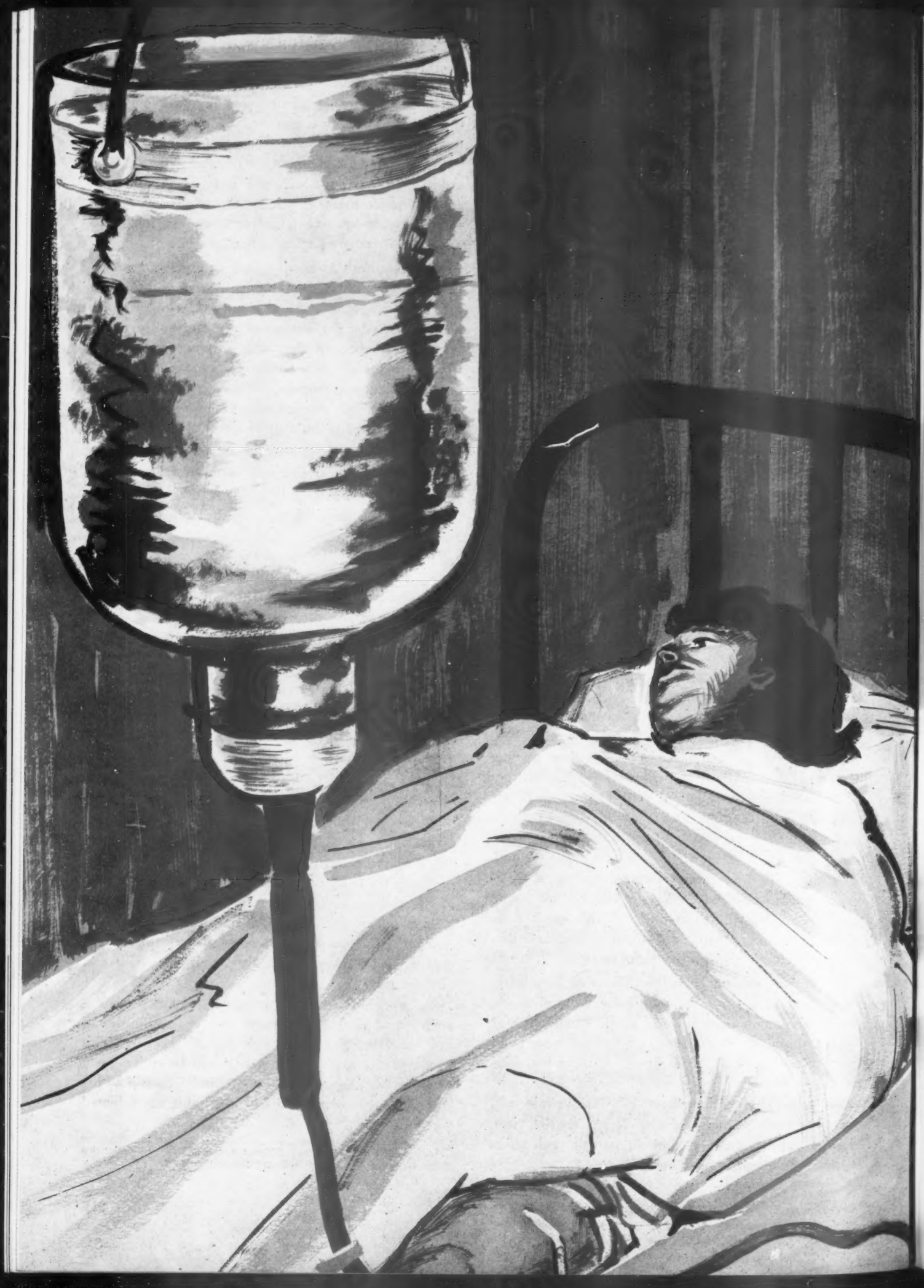
In closing, I would point out that I have purposely avoided discussing the secretary-stenographic position and the cashier post. These positions have duties so distinct and apart from the actual handling of medications that nothing is gained by a discussion of these positions in this paper.

Job Descriptions

A question that is constantly asked in discussions of this subject is that of how to write job descriptions. Job description writing is fairly simple if the three prerequisites to a good description are borne in mind in the writing process, namely, a description of the specific duties and responsibilities of the position; a description of the minimum level of performance expected; and a discussion of the knowledge, skills and abilities needed.

In conclusion, there is presented a typical job description, depicting the duties and responsibilities of the experienced pharmacy helper-storekeeper. This may serve as a guideline, should you be called upon to write this position for your hospital. Note how the three elements of a good job description are adhered to.

*Adapted from Pharmacy Helper series, U. S. Civil Service Commission—Class Specifications, December 1947.



use of the term

MILLIEQUIVALENT

in hospital pharmacy

by PAUL J. NIEBERGALL

► A PHARMACIST ON NIGHT CALL answered the telephone and was asked: "How many milliliters of a solution containing 40 milliequivalents of potassium per milliliter would I need to get three grams of potassium?" This and similar type questions concerning milliequivalent weights have been asked in hospitals with increasing frequency, indicating that medical schools are replacing older terms with milliequivalents in regard to electrolytic solutions. This trend has also been noted in the literature and on the labels of commercially prepared electrolytic solutions. The introduction of Ion-o-trate(Abbott) and Incert(Baxter). is rapidly bringing the day of tailor-made intravenous electrolyte solutions to the hospital. This trend by medical schools, research workers, and commercial companies toward using the term milliequivalents makes it imperative that hospital pharmacists become completely familiar with the term and its use in the preparation of intravenous electrolyte solutions.

Importance of Electrolytes

The body salts, or electrolytes, are of vital importance in maintaining the internal environment of our bodies. Some of the more important functions of electrolytes are the keeping of the body at a *p*H of 7.4, maintenance of osmotic pressure, and maintenance of neuromuscular activity. In addition, electrolytes help regulate the metabolism of the body. The chloride ion, in particular, is of vital importance in the exchange of oxygen and carbon dioxide between the red blood cells and the body cells.

Impairment of any one of the above functions leads to serious consequences, and could be fatal if not corrected. The loss of a cation such as sodium, for example, through diarrhea, can cause acidosis. The loss of an anion, such as chloride through vomiting, can cause alkalosis. Either of these losses might be fatal. These deficiencies can be corrected by using sodium lactate for the treatment of acidosis, and any chloride solution for the alkalosis. An overdose of either would, however, cause the opposite condition. It is therefore very important to replace the missing electrolytes as accurately as possible.

Milliequivalents vs Milligram Percent

Until recently laboratories have given reports of body electrolytes in terms of milligram percent(milligrams per 100 milliliters), and physicians have given the appropriate electrolytes in terms of milligram percent. For example, if the patient had an excess of 5 milligram percent of chloride, the physician would order 5 milligram percent of sodium lactate to balance the weight.

What is wrong with using milligram percent? The answer lies in the fact that we are comparing by weight two things which cannot be compared by weight. Chemically, electrolytes act quite differently from each other, and comparing them by weight

PAUL J. NIEBERGALL, B.S., is a Senior Pharmacy Intern in the University Hospital and a candidate for the degree of Master of Science in Pharmacy at the University of Michigan, Ann Arbor, Mich.

Table of Valence, Atomic or Formula Weights, and Milliequivalent Weights of Several Ions

Ions	Formula	Atomic or Formula Wt.	Valance	Milliequivalent Weight (mg.)
Sodium	$Na+$	22.997	+1	22.997
Potassium	$K+$	39.096	+1	39.096
Ammonium	NH_4+	18.04	+1	18.04
Magnesium	$Mg++$	24.32	+2	12.16
Calcium	$Ca++$	40.08	+2	20.04
Chloride	Cl^-	35.457	-1	35.457
Lactate	$CH_3CH(OH)COO^-$	89.07	-1	89.07
Monohydrogen Phosphate	$HPO_4=$	95.988	-2	47.994
Sulfate	$SO_4=$	96.066	-2	48.033

Table of Factors for Conversion of Milligrams Percent to Milliequivalents

Ions	To convert mg.% to mEq./L. Divide by:	To convert mEq./L. to mg.% Multiply by:
Sodium	2.30	2.30
Potassium	3.91	3.91
Ammonium	1.80	1.80
Magnesium	1.22	1.22
Calcium	2.00	2.00
Chloride	3.55	3.55
Lactate	8.91	8.91
Phosphate	4.80	4.80
Sulfate	4.80	4.80

Normal Body Electrolyte Concentrations

Extracellular				Intracellular			
mEq./L. plasma				mEq./L. intracellular water			
Cations		Anions		Cations		Anions	
Na	142	Cl	104	K	150	HCO_3	10
K	4.5	HCO_3	29	Na	10	Cl	2
Ca	5	SO_4	1.5	Mg	40	HPO_4	88
Mg	3	HPO_4	2			Protein	80
		Org. acids	2			SO_4	20
		Protein	16				

would be the same as saying that car engine A is as powerful as car engine B, because they each weigh the same. We know, however, that although the car engines might weigh the same, engine A might have 200 H.P. as compared to engine B having 100 H.P. Comparing the engines through a meaningful common denominator such as horse-power would tell us that car engine A is twice as powerful as car engine B although they weigh exactly the same.[1] Just as weight will not tell us how powerful an engine is, so it will not tell us how powerful different electrolytes are.

The important difference between automobile engines is not weight but horse-power, and likewise the important difference between electrolytes is not weight *but combining power*. There is a denominator common to all chemical reactions which can be used to evaluate the power of electrolytes. This common denominator is the hydrogen ion, formed when atoms of hydrogen come into contact with water.

Valence

In order to understand how the hydrogen ion acts as the common denominator in chemical reactions we must go back to the basic unit of structure, the atom, which is itself composed of smaller units. The essential units for the understanding of chemical reactions, and milliequivalents, are the proton and the electron. The proton, or positive charge is concerned with the weight of the atom, while the electron, or negative charge determines the type of reaction any particular atom will undergo. It is through donating, sharing, or accepting electrons that chemical reactions take place. The capacity of any atom to donate, share, or accept electrons is known as valence.[2] The valence of an element is designated by a whole number preceded by a plus or minus sign. An element with a plus valence will accept electrons, while an element with a negative sign will donate electrons. In order for a stable compound to result from a reaction, the number of electrons donated, shared or accepted must result in a neutral charge. For example:

1. One atom of hydrogen can combine with one atom of chlorine to form one molecule of hydrogen chloride. In this reaction hydrogen, which requires one electron to form a stable compound, receives the electron from the chlorine which has one surplus electron. Hydrogen, because it receives one electron, has a valence of plus one. Chlorine, because it donates one electron, has a valence of minus one.

2. Calcium can combine with chlorine to form calcium chloride. However, calcium has a surplus of two protons and, therefore, needs two electrons to become neutral, thus forming a stable compound. Since each chlorine atom can supply only one electron, it

takes two chlorine atoms to neutralize the plus two charge on the calcium atom. Since calcium has the capacity to accept two electrons, it has a valence of plus two.

In like manner an atom of an element with a valence of plus three would react with three atoms of an element with a valence of minus one, since each atom of the minus one valent element could supply only one of the needed three electrons.

Hydrogen Ion and Valence

Ions are formed when atoms of elements come into contact with water. The simplest of these is the hydrogen ion, designated as H^+, because it has a valence of plus one. This ion has one proton and requires one electron to become stable. Because of this it can be stated that in chemical reactions one H^+ is equivalent to one electron. Therefore valence can also be stated as the number of H^+ that will combine with or be displaced by one atom of the element in question.[3] In the second example given above, one atom of calcium, because it requires two electrons with each electron being equivalent to one H^+, can be said to be equivalent to two H^+.

Atomic Weight

One more term necessary for our discussion is atomic weight (A.W.) This is the relative weight of an element in relation to oxygen, which has an atomic weight of 16. Oxygen was chosen as the standard because it would simplify the calculation of all other atomic weights. The atomic weight shows the comparative weights between the elements, and can therefore be expressed in any unit of weight, the most common being gram.

Milliequivalent Weight

We have discussed why we use the term milliequivalent, now let us find out what is meant by it. One milliequivalent weight (mEq.) is 1/1,000 of an equivalent weight. One equivalent weight (E.W.) of an element is that weight of the element which will react with or displace one atomic weight of hydrogen expressed in grams.[3] The atomic weight of hydrogen is 1, so the equivalent weight of chlorine, for example, would be that weight of chlorine in grams which will react with one gram of hydrogen. We have shown above that one atom of chlorine is equivalent to one atom of hydrogen. One atom of chlorine with a valence of minus one and an atomic weight of 35 expressed in grams weighs 35 grams. One atom of chlorine weighing 35 grams reacts with one atom of hydrogen weighing one gram. The equivalent weight of chlorine is therefore 35 grams.

Calcium has a valence of plus two and is equivalent to two hydrogen atoms. Each hydrogen atom can be said therefore to be equal to half a calcium atom. One atom of hydrogen with atomic weight 1, expressed as 1 gram can then react with half a calcium atom (A.W. 40), each atom of calcium weighing 40 grams. One gram of hydrogen therefore reacts with 20 grams of calcium, making the equivalent weight of calcium 20. We can sum this as follows:

Equivalent weight equals the weight of one atom of the element expressed in grams, divided by the number of hydrogen atoms which will combine with or be displaced by one atom of the element.

This definition may be represented by the equation:

$$\text{E.W.} = \frac{\text{A.W.}}{\text{V}}$$

where E.W. is the equivalent weight expressed in grams, A.W. the atomic weight of the element, and V the valence. We find milliequivalent weight by dividing this number by 1,000, thus giving us our milliequivalent weight expressed in milligrams.

EXAMPLES

1. $\text{E.W. Chlorine} = \frac{\text{A. W. Chlorine}}{\text{Valence Chlorine}} = \frac{35}{1} = 35 \text{ Gm. or}$

$$\text{milliequivalent weight of chlorine} = \frac{35 \text{ Gm.}}{1000} = 35 \text{ mg.}$$

2. $\text{E.W. Calcium} = \frac{\text{A.W. Calcium}}{\text{Valence Calcium}} = \frac{40}{2} = 20 \text{ Gm. or}$

$$\text{milliequivalent weight of calcium} = \frac{20 \text{ Gm.}}{1000} = 20 \text{ mg.}$$

Problems Involving Milliequivalent Weight

We can now answer the question put to the pharmacist which appeared in the first sentence of this discussion.

How many milliliters of a solution containing 40 milliequivalents of potassium per milliliter would I need to have 3 grams of potassium?

From Table 1 we find the milliequivalent of potassium to be 39 milligrams. If the solution contains 40 milliequivalents per milliliter, we then have 40 x 39 or 1,560 milligrams of potassium per milliliter. We can change this to grams and divide into 3 grams giving us the answer of 1.9 milliliters of solution needed to supply 3 grams of potassium.

$$\frac{\text{Weight needed expressed in mg.}}{\text{mEq./ml. x milliequivalent weight}} = \text{ml. of solution}$$

To change milligram percent to milliequivalents per liter, we use the following formula:

$$\text{mEq. per L} = \frac{\text{mg. per 100 ml. x 10 x valence}}{\text{A.W.}}$$

Using this same formula, but changing it around we can convert milliequivalents per liter into milligram percent:

$$\text{mg. percent} = \frac{\text{mEq. per L. x A.W.}}{\text{valence x 10}}$$

We used milliequivalents per liter in this example because the physician usually prescribes electrolyte solutions by the liter, and would rather know the total number of milliequivalents per liter rather than the number of milliequivalents per milliliter. It is simply a matter of convenience.

Preparation of Solutions

In preparing a solution of potassium, we can dissolve a salt of potassium in water. When we dissolve a salt to make an electrolyte solution, we must remember that in addition to the element that we want, we also have at least one element of the opposite valence. Since the two elements in the salt are chemically equal, the milliequivalents of one must be equal to the milliequivalents of the other. If we dissolved enough potassium chloride in water to give us 40 milliequivalents per liter of potassium, we would also have *exactly* 40 milliequivalents per liter of chloride ion. We *do not* have a solution containing 40 milliequivalents of potassium chloride. The solution is designated as having 40 milliequivalents of K^+ and 40 milliequivalents of Cl^- per liter.

A solution containing the same number of milliequivalents of each ion does not contain the same weight of each ion. Let us use our solution containing 40 milliequivalents of K^+ and 40 milliequivalents of Cl^- per liter.

40 mEq. K^+ = 40 x 39 mg. = 1560 mg. K^+ per liter
40 mEq. Cl^- = 40 x 35 mg. = 1400 mg. Cl^- per liter

From this we can see why comparing electrolytes by weight is misleading. If we were comparing the ions K^+ and Cl^- by weight in the above solution, we would say that we had more potassium in the solution. However, as far as chemical reactions go, and as far as our bodies would be concerned if we needed these ions, the above solution would contain exactly the same amount of K^+ and Cl^-.

Calculations Involved in Preparing Electrolyte Solutions

Dissolving a salt in water to form an electrolyte solution necessitates the use of molecular weights (M.W.) in our calculations. The molecular weight of a compound is the sum of the atomic weights of all of the elements of that compound. We can calculate the molecular weight of any compound by adding the atomic weight of each element as many times as that element appears in the compound. The molecular weight of sodium chloride would be:

A.W. Sodium (23) + A.W. Chlorine (35) = 58

We can find the molecular weight of any official compound in the *U.S.P.* or *N.F.*, or in the *Merck Index.* If the compound is not official, *Merck Index* would have it listed under the individual compound.

EXAMPLES

1. Prepare a solution containing 154 milliequivalents per liter of Na^+ using sodium chloride. How much sodium chloride would be needed?

$$\text{Wt. of salt} = \frac{\text{mEq. per liter of desired ion x M.W. of salt in mg.}}{\text{valence of highest valent element x 1000}}$$

$$\text{Wt. sodium chloride} = \frac{154 \times 58.45}{1 \times 1000} = \frac{9001.30}{1000} = 9 \text{ Gm. NaCl}$$

2. Using the same formula turned around, we can find the number of milliequivalents per liter of any ion if we know the concentration of the solution or the weight of the salt in the solution.

A solution contains 9 grams of sodium chloride in 1,000 milliliters. How many milliequivalents per liter of Na^+ are there?

$$\text{mEq. per liter} = \frac{\text{Wt. of salt x valence of highest valent ion x 1000}}{\text{M.W. of the salt}}$$

$$\text{mEq. per liter of } Na^+ = \frac{9 \times 1 \times 1000}{58.45} = \frac{9000}{58.45} = 154 \text{ mEq. per liter } Na^+$$

Conclusion

The preparation of any electrolyte concentration should be but a matter of minutes if the basic formula $\text{E.W.} = \frac{\text{A.W.}}{\text{Valence}}$ is remembered. From this can be derived all of the other equations presented, and any which may be needed in the future. The use of milliequivalents, once mastered, can be of invaluable assistance to the hospital pharmacist interested in giving better pharmaceutical service. Electrolyte solutions are here to stay, and the hospital pharmacist should be able to prepare solutions which are not commercially available, and to change the concentration of solutions as the need arises.

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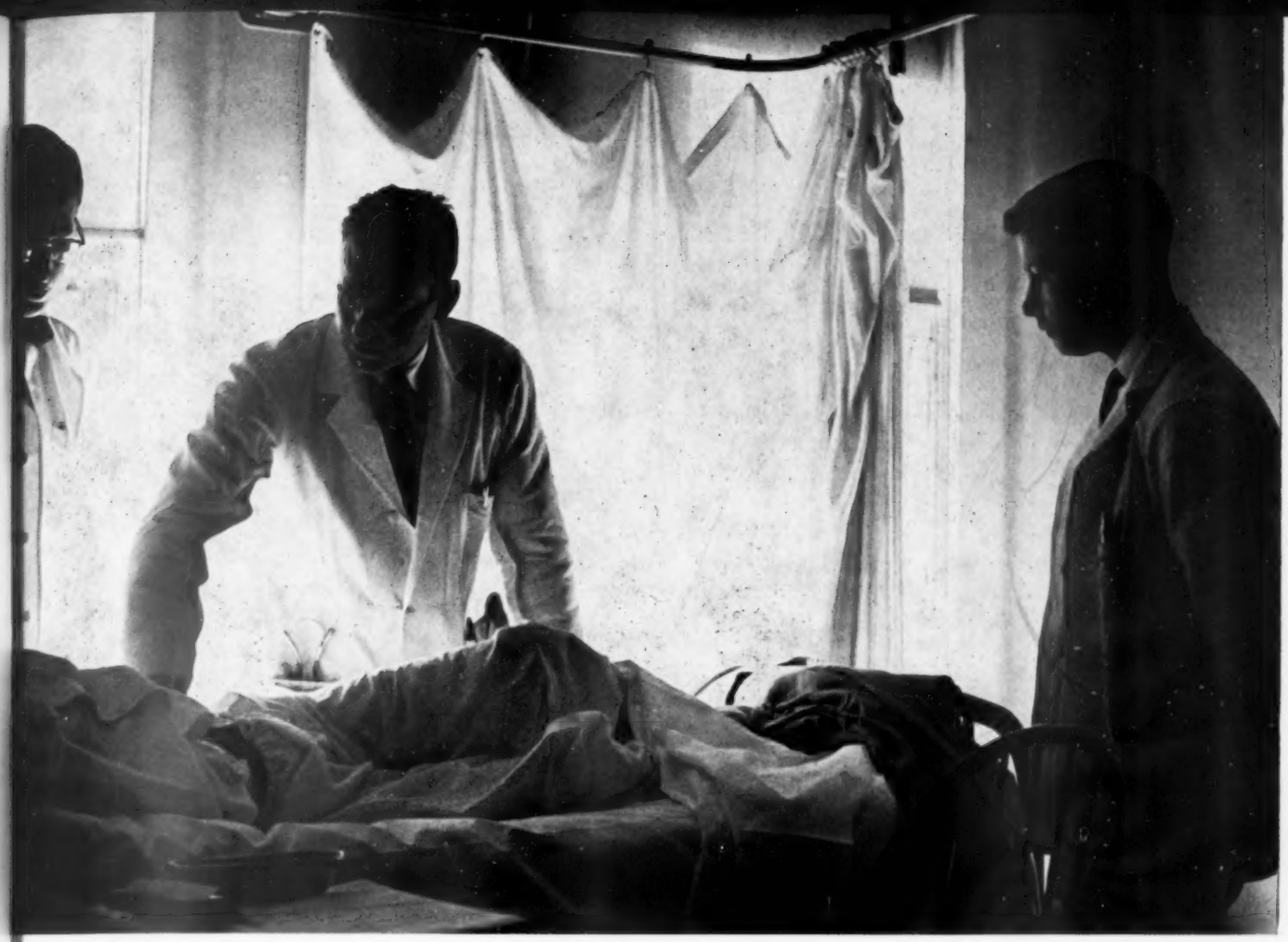

evaluation of a NEW DEODORANT

for use in hospitals

by NEAL SCHWARTAU

► THE EXISTENCE OF DISAGREEABLE ODORS in the hospital is a constant problem. Many of the deodorants that have been used previously were based on formaldehyde which acts by paralyzing the sense of smell. A new product is now available which is very effective and which does not have the disadvantages of the older deodorants.

This product, Magnador Deodorant 41*, was originally developed for use in restaurants where it was desirable to mask cooking and frying odors and at the same time not destroy the customers' ability to enjoy the aroma of the food being served them.

The product is a thick amber-colored liquid which must be diluted for use. Various dilutions of this deodorant were tried in our hospital for use in the familiar wick-type deodorant bottles. The 1:20 dilution with water was found to be the most effective in all cases. The deodorant bottles are used in all public toilets and in any patients' rooms where a deodorant is necessary. It was found to be particularly effective in combating the odors associated with terminal carcinoma cases.

The 1:20 dilution was also used in the scrub water used in cleaning patients' rooms and other areas where a residual odor persists. For this purpose an ounce is added to the average size pail.

In all cases the deodorant leaves a clean, fresh odor which has not been disagreeable to any patient or employee.

The product is very economical. A gallon of the 1:20 dilution can be prepared for a cost of 75 to 80 cents.

NEAL SCHWARTAU is Chief Pharmacist at the Rochester Methodist Hospital, Rochester, Minnesota.

*Manufactured by Magnus, Mabee, and Reynard.

HYPODERMIC SYRINGES and HIGH-FREQUENCY SOUND

by HAROLD M. BEAL and DONALD M. SKAUEN

►FOR MANY YEARS HIGH-FREQUENCY SOUND has been employed as an acceptable parts-cleaning device in production processes. Very recently, interest in cleaning surgical instruments and glassware by ultrasonics has resulted in the development of specialized instruments for this purpose.

This research was undertaken to compare ultrasonic cleaning of hypodermic syringes with conventional methods. Since in the majority of the syringes obtained for this study, the plunger could not be separated from the barrel, it was decided to explore the ultrasound method for releasing frozen syringes as well.

Equipment

Generator. The ultrasonic generator used in this study was a Sonogen apparatus, Model AP-25-B connected to a T-52 transducer manufactured by the Branson Ultrasonic Corporation, Stamford, Connecticut. The barium titanate transducer operates at a frequency of 38 KC, is housed in all welded stainless steel, and has a liquid capacity of about 2 gallons. It is of sufficient size to insonate 50 or more syringes simultaneously.

Syringes. All of the syringes used in this study were obtained from the Hartford Hospital, Hartford, Connecticut. Syringe sizes varied from 1 ml. to 50 ml.

Syringe Opener. The syringe opener was a standard Becton-Dickinson model.

Purity Meter. For testing conductance of water in the cleaning operation a Barnstead Purity Meter, Model PM-2 was used.

Experimental Freeing of Frozen Syringes

Solvent System. To discover the most appropriate solvent system for freeing "frozen" syringes, ten syringes were immersed in the solvent in the tank and insonated for a 10-minute period. The syringes were then removed from the tank and the number whose parts could be separated were recorded. The following solutions were screened by this method: 2 percent citric acid solution; 2 percent citric acid and 0.5 percent Alconox[1] solution; Zephiran solution,[2] 1:5000; Zephiran solution 1:1000; 2 percent sodium citrate solution; 2 percent sodium citrate and 0.5 percent Tween-80[3] solution; 1 percent Nacconol[4] NRSF solution; and 1 percent Duponol C[5] solution. Because Duponol C and Nacconol NRSF freed a much higher percent of syringes, they were employed for the remainder of the study.

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Presented at the Section on Hospital Pharmacy of the Fourth Pan-American Congress of Pharmacy and Biochemistry, Washington, D. C., November 6, 1957.

Methodology

Methodology. From the experience gained in the solvent screening program a method evolved for comparing ultrasonic freeing of syringes with standard techniques. Nacconol NRSF one percent solution was injected into the opening in each syringe, the syringe opener filled with warm water, attached to the syringe, and pressure applied. Syringes resisting this treatment were then placed into the tank of the generator containing 1 percent Nacconol NRSF at about 120° F. and insonated for 10 minutes. At the end of this period the syringe opener was again applied and results recorded.

A group of syringes was obtained which had resisted the usual hospital freeing operation and had been discarded. The

TABLE 1. RESULTS OF SUBJECTING SYRINGES RESISTANT TO HOSPITAL PROCEDURES TO INSONATION FOR 10 MINUTES AT 120° F. IN NACCONOL NRSF 1% SOLUTION

SYRINGE OPENER ONLY	INSONATED 10 MINUTES	REMAINING FROZEN	TOTAL
8	6	9	23
8	14	11	33
26	13	4	43
41	13	18	72
83	46	42	171
48% of total	27% of total	25% of total	

1. Alconox, Inc., Jersey City, New Jersey
2. Winthrop Chemical Co., New York, New York
3. Tween 80 Atlas Powder Co., Wilmington, Delaware
4. Nacconol NRSF, National Aniline and Chemical Co., New York, N. Y.
5. Duponol C; Dupont Company

Sonogen Ultrasonic Generator

TABLE 2. RESULTS OF SUBJECTING FROZEN SYRINGES, PREVIOUSLY UNTREATED, TO INSONATION FOR 10 MINUTES AT 120° F. IN DUPONOL C 1% SOLUTION.

OPENER ONLY	INSONATED 10 MINUTES	REMAINING FROZEN	TOTAL
10	16	2	28
—	19	3	22
—	24	3	27
10	59	8	77
13% of Total	77% of Total	10% of Total	

above procedure was applied to these and the results are recorded in Table 1.

Another group of syringes which had not been subjected to hospital freeing methods was obtained. The first 28 of these were processed as above and results recorded in Table 2. The remainder were insonated without first subjecting them to the syringe opener since the only important figure required was that of the total number of freed syringes. These totals also appear in Table 2.

All syringes resistant to the above treatment were then placed in the tank and irradiated for one hour, to determine if prolonged ultrasonic action would have any effect. Results of this insonation appear in Table 3.

Discussion

It will be noted that results recorded in Table 1 appear to be less favorable than Table 2. This is easily explained on the basis of a much more resistant syringe. Because of this fact the high percentage of syringes freed by only 10 minutes of insonation is indeed significant.

The data appearing in Table 2 is more nearly what would be expected if this procedure were to be fol-

TABLE 3. RESULTS OF INSONATION FOR 1 HOUR OF ALL PREVIOUSLY RESISTANT SYRINGES

INSONATED - 1 HOUR	REMAINING FROZEN
36	10

lowed in a central sterile supply. The low percentage of syringes resistant to this treatment indicates that ultrasound has marked usefulness in such cases.

Perhaps the most significant fact reported is that of the 248 frozen syringes studied, only 10 were resistant to the procedure developed in this research. It is highly possible that further insonation would decrease this number even more.

Inasmuch as this method of freeing syringes is very simple, rapid and economical, it would seem likely that central sterile supply laboratories might incorporate it in their procedures. The savings in discarded syringes alone in some hospitals would warrant careful consideration of purchasing such an instrument.

Cleaning Syringes

The development of a technique to evaluate cleaning efficiency of ultrasound for glass syringes has proven to be a more formidable task.

Preliminary experiments indicate that a 5 minute insonation period would be sufficient for comparison with hand cleaning techniques and that a 1 percent Duponol C solution could be used as the standard detergent.

Procedure

The method utilized for cleaning the soiled syringes was to place them in the tank containing the 1 percent Duponol C at 120° F, insonate for 5 minutes, remove from the tank, rinse with water and then with distilled water.

Comparison with Other Cleaning Methods

Visual observation of the ultrasonically cleaned syringes in most cases gave an impression of superior cleansing power. The metal hubs were brighter and the glass more transparent than those subjected to standard central supply cleaning or hand cleaning. The authors felt that a more precise measurement of cleaning power should be employed and the following experiments were carried out to this end.

Optical Density

Ten syringes cleaned with the Sonogen, 10 by hand and 10 in the hospital central supply, were soaked in distilled water in a beaker. A sample of the water from each beaker above was placed in a "Lumetron Colormeter" and densities compared. All readings were identical.

Ion Exchange

The distilled water from the foregoing procedure was passed through an ion exchange column containing IRC-120[1] with the thought that sufficient ions might be present to be absorbed on the column. The columns were eluted with HCl, the eluate evaporated, with no significant extraction having taken place.

Conductance

Using the Barnstead Purity Meter for testing conductance of the water in which cleaned syringes had been macerated, also provided inconclusive results. These are recorded in Table 4.

Table 4. Purity Meter Readings of Extractions after Various Cleaning Processes

	Reading in parts per million
Distilled Water	0.5
Insonated Water	0.5
Hospital Cleaned Syringe Extract	0.75
Hospital Cleaned Syringes Insonated then Extracted	0.80
Hand Cleaned Syringe Extract	0.45
"Sonogen" Cleaned Syringe Extract	0.50
Hand Cleaned Syringes - Macerated for 10 min. at 90° C.	0.60
"Sonogen" Cleaned Syringes Macerated for 10 min. at 90° C..	0.75

Discussion

Although visual observation indicated superior cleaning characteristics, this cannot be supported by any of the experiments conducted to date. On the other hand, from data collected it can be stated that ultrasonic cleaning of syringes is just as effective as certain other cleaning techniques. Rapidity of cleaning is also a factor in favor of high-frequency cleaning methods.

The authors intend to carry this research one step further and employ radioactive procedures in order to satisfy themselves of the relative value of ultrasonic cleaning when compared with conventional methods.

Summary

1. An ultrasonic method for releasing frozen syringes has been developed.

2. The ultrasonic method for release of frozen syringes is superior to conventional methods from the point of view of speed, manual labor, economy, and saving of syringes.

3. Ultrasonic cleaning of hypodermic syringes is comparable with usual central sterile supply procedures. Using high-frequency sound techniques it is quite likely that savings in time can be demonstrated.

1. Rohm & Haas, Philadelphia, Pennsylvania

INJECTION TRAUMA

MORE OR LESS?

by RANDALL B. TINKER and RICHARD A. HILL

► IT HAS BEEN REPORTED PREVIOUSLY that disposable hypodermic needles possess significant advantages over the conventional needles.[1] Serum hepatitis in particular has been traced to reusable needles which have been improperly reprocessed and resterilized. The use of disposable hypodermic needles *obviates cross-infection possibility* through this particular medium. Reusable needles demand extensive handling throughout the cycle of reprocessing, use and return to the central sterile supply area. Use of disposable needles *eliminates* much of this *time-consuming effort* and *frees nursing personnel* for other endeavors. *Good patient psychology is assured* by destroying the new type needle in the patient's presence after the injection of medication has been made. Modern engineering and production advances have made the disposable needle an economic feasibility.

There is, however, an additional factor which deserves examination: the effect of needle sharpness upon the physical comfort of the patient.

Physical discomfort of injections is closely allied with the sharpness of the point of the hypodermic needle being used.[2] Tissue trauma from a dull or burred needle causes frequent complaint by patients; yet, the presence of a burr on the reusable needle is the only generally recognized standard for resharpening. Consideration has not been given ordinarily to the wear that a needle point undergoes during the cycle of use, cleaning and reprocessing in the central sterile supply area. This study was undertaken, therefore, to determine the effect of such reprocessing, and to determine if this effect produces a dulling of the needle to an extent which would imply patient discomfort. It should be noted also that it is an accepted medical fact that infections are more prone to develop in traumatized puncture wounds than in similar but sharply incised wounds.

Experimental Methods

For the purposes of this investigation needles of 20, 23 and 25 gauge were considered to be representative of the sizes most commonly used in the hospital for general parenteral administration of medication.

Conventional needles representing five brands from four manufacturers were obtained through commercial sources, utilizing more than one wholesaler in order to obtain representative sampling of several lots of each manufacturer's needles.

Needle sharpness was measured by the amount of pressure required to cause the needle to penetrate a standardized diaphragm. This procedure has been recognized as being indicative of sharpness. Using the penetration pressure value (penetration index) required by the needle in a new condition as the base, the increase in the pressure required for penetration of the diaphragm was recorded and calculated as a percentage change in comparison to the established base.

Four-hundred fifty needles (divided into 3 groups of 150 needles each[a]) were used in the collection of the data. One

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Presented before the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, New York, N. Y., April, 1957.

TABLE 1

PERCENTAGE INCREASE IN PENETRATION INDEX FOR FIVE BRANDS OF 25 GAUGE HYPODERMIC NEEDLES AFTER (1) AUTOCLAVING, (2) HOSPITAL PROCESSING, AND (3) INJECTION PLUS HOSPITAL PROCESSING

No. of Cycles	Autoclaving Brand					Hospital Processing Brand					Injection plus Processing Brand				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
1	13.4	15.8	5.4	1.7	19.0	23.7	32.0	21.2	26.6	28.8	42.0	43.1	30.2	38.2	46.6
2	28.6	32.6	0.0	5.9	30.0	47.6	51.2	37.9	38.4	51.3	84.2	86.8	69.6	68.6	85.6
3	42.0	47.8	-5.4	2.5	39.1	67.0	77.8	48.7	47.2	60.1	87.5	88.1	72.2	74.1	88.4
4	52.6	58.6	-7.7	3.4	46.9	76.3	82.3	56.2	58.3	68.9	89.0	90.6	74.6	77.3	90.2
5	53.6	63.1	-1.5	2.5	53.0	83.9	84.2	65.5	67.9	82.8	90.2	92.2	75.3	80.1	93.1

TABLE 2

PERCENTAGE INCREASE IN PENETRATION INDEX FOR FIVE BRANDS OF 23 GAUGE HYPODERMIC NEEDLES AFTER (1) AUTOCLAVING, (2) HOSPITAL PROCESSING, AND (3) INJECTION PLUS HOSPITAL PROCESSING

No. of Cycles	Autoclaving Brand					Hospital Processing Brand					Injection plus Processing Brand				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
1	9.8	10.7	6.0	1.2	10.0	23.7	29.6	20.2	22.6	17.6	28.7	45.6	31.6	32.2	37.0
2	27.2	29.3	1.3	-1.2	10.4	42.5	40.8	42.6	45.3	42.2	78.6	82.4	64.2	67.1	61.8
3	43.9	45.6	-4.0	0.0	18.4	55.4	75.2	54.2	56.2	46.9	80.1	86.1	66.8	70.0	63.8
4	50.6	53.8	-5.2	-1.7	18.4	71.2	79.6	58.8	58.8	51.4	85.0	87.6	67.9	72.2	66.1
5	51.5	55.1	-2.0	1.7	19.9	74.2	80.9	62.3	64.1	55.0	86.2	89.1	70.6	73.8	68.6

TABLE 3

PERCENTAGE INCREASE IN PENETRATION INDEX FOR FIVE BRANDS OF 20 GAUGE HYPODERMIC NEEDLES AFTER (1) AUTOCLAVING, (2) HOSPITAL PROCESSING, AND (3) INJECTION PLUS HOSPITAL PROCESSING

No. of Cycles	Autoclaving Brand					Hospital Processing Brand					Injection plus Processing Brand				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
1	7.1	8.8	6.2	5.1	17.7	23.7	20.2	18.8	20.2	26.2	27.9	40.2	32.1	33.6	43.2
2	21.4	26.7	2.8	2.0	28.4	43.1	43.0	38.2	38.6	48.4	76.4	72.8	69.2	69.8	71.9
3	39.5	40.2	-8.5	4.6	28.4	53.2	62.6	42.1	43.8	60.2	79.6	75.1	70.8	72.1	74.1
4	44.5	46.3	-9.6	8.3	31.6	61.1	66.4	45.8	46.3	64.0	82.4	76.6	72.6	73.8	76.4
5	45.6	49.1	-4.0	6.1	36.7	62.6	69.0	50.1	52.6	67.1	84.1	78.1	73.0	74.2	78.8

group received an initial ether rinse followed by autoclaving at 15 lbs./in.^{2} for 30 minutes. A second group received routine hospital processing, *i.e.* water rinse, detergent soak, styletting, cleansing of the hub with a cotton-tipped applicator, water rinse, ether rinse, and autoclaving. The third group were used to inject 2 ml. of Water for Injection into the shaved abdomen of anesthetized rats[3] prior to routine hospital processing. Penetration pressures were measured for group one immediately after each of the autoclaving cycles; for group two, immediately after the autoclaving in the hospital processing cycle; and for the third group, immediately prior to injection. The cycles were repeated four times.[b]

Data and Discussion

The results obtained from each of the three gauges of needles are reported in Tables 1, 2, and 3.

The data in Table 1 show that three brands of needles required progressively more pressure for penetration after each autoclaving. Two brands, however, appeared to be little affected by the autoclaving cycles. The absence of significant change in pressure requirement for penetration in these two brands is apparently due to the buffing compound or surface treatment employed. Brands 3 and 4 are shown to be dulled to a lesser degree than the other brands tested. The data further show that the treatments investigated tend to dull all hypodermic needles in a progressive manner.

Examination of the data presented in Tables 2 and 3 indicate similar findings for 23 and 20 gauge needles, respectively.

Table 4 represents the average values obtained when all the recorded values for each gauge needle were taken into consideration. These data are graphically represented in Figures 1, 2, and 3.

It is apparent, therefore, that hospital processing and injection do produce appreciable changes in sharpness not readily detected by gross visual examination. These changes are shown to be quantitative, dulling needles to the extent that approximately 70 percent more pressure is required for penetration (all gauges

[a]Thirty needles from each of five manufacturers composed each group.

[b]The cooperation of the staff of Alachua General Hospital is gratefully acknowledged.

Figure 1- PERCENTAGE INCREASE IN PENETRATION INDEX OF 25 GAUGE HYPODERMIC NEEDLES AFTER (1) AUTOCLAVING, (2) HOSPITAL PROCESSING, AND (3) INJECTION PLUS HOSPITAL PROCESSING.

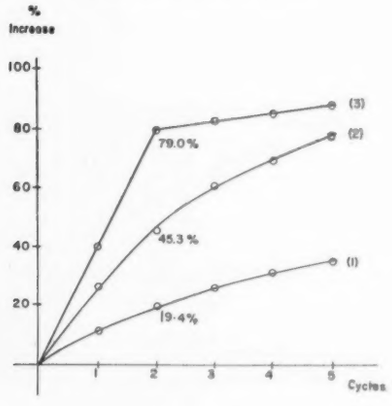


Figure 2- PERCENTAGE INCREASE IN PENETRATION INDEX OF 23 GAUGE HYPODERMIC NEEDLES AFTER (1) AUTOCLAVING, (2) HOSPITAL PROCESSING, AND (3) INJECTION PLUS HOSPITAL PROCESSING.

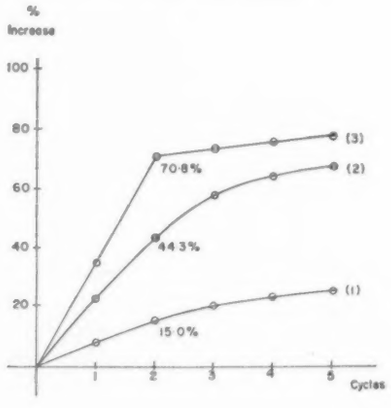


Figure 3- PERCENTAGE INCREASE IN PENETRATION INDEX OF 20 GAUGE HYPODERMIC NEEDLES AFTER (1) AUTOCLAVING, (2) HOSPITAL PROCESSING, AND (3) INJECTION PLUS HOSPITAL PROCESSING.

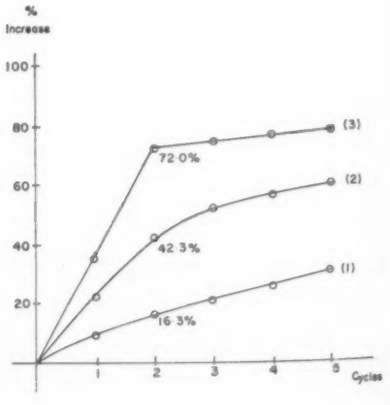


TABLE 4

AVERAGE PERCENTAGE INCREASE IN PENETRATION INDEX FOR FIVE BRANDS OF HYPODERMIC NEEDLES AFTER (1) AUTOCLAVING, (2) HOSPITAL PROCESSING, AND (3) INJECTION PLUS HOSPITAL PROCESSING. (25, 23 AND 20 GAUGE)

Cycles	25 Gauge	23 Gauge	20 Gauge
	Autoclaving		
1	11.1	7.5	9.0
2	19.4	15.0	16.3
3	25.2	20.8	20.8
4	30.8	23.2	24.2
5	34.1	25.2	26.7
	Hospital Processing		
1	26.5	22.7	21.8
2	45.3	44.3	42.3
3	60.2	57.6	52.4
4	68.4	64.0	56.7
5	76.9	67.3	60.3
	Injection plus Processing		
1	40.0	35.0	35.4
2	79.0	70.8	72.0
3	82.1	73.3	74.3
4	84.3	75.8	76.2
5	86.2	77.7	77.6

considered) after only two cycles of use. It is reasonable, therefore, to believe that this adds to patient discomfort and increases the possibility of trauma.

Under ideal conditions needles should be withdrawn for resharpening after the second injection. However, barring the development of a burr, the conventional reusable needle is used frequently as many as 10 to 15 times prior to being resharpened. After such extended use, the penetration pressure values will have increased nearly 100 percent over the initial pressure required for tissue penetration.

TABLE 5

RELATIVE SHARPNESS OF VARIOUS GAUGES OF HYPODERMIC NEEDLES FROM SEVERAL MANUFACTURERS

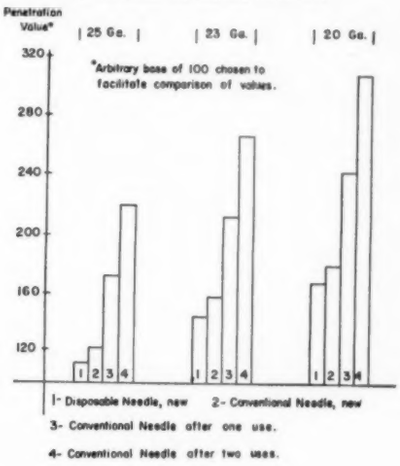
Brand	Type	Relative Sharpness Referred to Base 100 25 Gauge	23 Gauge	20 Gauge
1	Conventional	130	156	170
2	Conventional	130	173	196
3	Conventional	129	152	177
4	Conventional	114	169	169
5	Conventional	112	134	182
	Average - - - - -	123	157	179
6	Disposable	118	149	171
7	Disposable	107	138	163
	Average - - - - -	113	144	167

A comparative investigation of the sharpness of conventional needles and disposable needles is reported in table 5. Comparison of results was facilitated by the adoption of an arbitrary base of 100. Each figure recorded represents the average value of 5 penetrations for each of 10 individual needles of a particular size and brand.[c]

[c]These data represent needles of six manufacturers. Inasmuch as one manufacturer produces both conventional and disposable needles and another manufacturer produces two brands of conventional needles, this method of data presentation was adopted in order to conceal manufacturers' identities.

Examination of the above data indicates that disposable needles are equal to, if not superior to, conventional needles when new. Bar graphs 1 and 2 in Figure 4 represent average sharpness values of disposable and conventional needles as taken from the data in Table 5. Bar graphs 3 and 4 represent the calculated values for conventional needles after one and two cycles of use, respectively. The calculation was based on the average penetration value of the conventional needle when new, increased by the percentages reported in Table 4 for one and two use cycles, respectively.

Figure 4- COMPARISON OF SHARPNESS OF DISPOSABLE AND CONVENTIONAL HYPODERMIC NEEDLES.



Examination of the data presented in Figure 4 shows that disposable hypodermic needles are on the average sharper than conventional needles and from this it is evident that the disposable needle tends to reduce tissue trauma and to increase patient comfort.

Summary

Conventional hypodermic needles have been shown to require as much as 70 percent more pressure for penetration after two cycles of hospital use.

Disposable hypodermic needles have been shown to be consistently sharper than conventional needles in a new condition, thereby causing the patient a minimum of discomfort.

Disposable hypodermic needles, due to their sharpness, reduce the hazards of tissue trauma and thus of injection abscesses.

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1. Tinker, R. B.: A Case for Disposable Hypodermic Needles, *Bull. Am. Soc. Hosp. Pharm. 13*:319 (July-Aug.) 1956.

2. Franz, F. and Tovell, R. M.: A Study of Hypodermic Needle Points, *Anesthesiology 17*:724 (Sept.-Oct.) 1956.

3. Harry, R. G.: *Modern Cosmeticology*, Chemical Publishing Co., Inc., Brooklyn, 3rd rev. ed., 1947. Pp. 92-93.

Revised

MINIMUM STANDARD FOR PHARMACY INTERNSHIP

in hospitals

I. Definition

A pharmacy internship in a hospital is a post-graduate program of organized training, approved by the Division of Hospital Pharmacy of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. This training shall consist of not less than 2,000 hours extending over a period of at least one year.

Guide to Definition

Approval of hospital pharmacy internship programs shall be in compliance with criteria promulgated by the Division of Hospital Pharmacy of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The hospital administrator or the pharmacist in charge shall make application for such approval to the Division of Hospital Pharmacy of the American Pharmaceutical Association, 2215 Constitution Avenue, N.W., Washington 7, D. C.

The pharmacist in charge of the hospital pharmacy shall be the director of the internship training program and shall be subject to similar overall administrative control and guidance employed by the hospital for medical, dental, dietetic and other similar internships.

Internship training should extend over a period of 50 weeks or longer and under no circumstances shall it be less than 48 weeks.

II. Qualifications of the Training Hospital

The hospital shall be a general hospital accredited by the Joint Commission on Accreditation of Hospitals and meeting in full the pharmacy elements of the accreditation schedule. In addition, the hospital must

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Revised by the Committee on Minimum Standards of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS composed of Clifton J. Latiolais, *Chairman,* Sister Mary Florentine, George F. Archambault, Jeannette Sickafoose, and John Webb.

This revised standard was presented and adopted at the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS in New York May 1957.

be approved for medical internship training by the Council on Medical Association. Pharmacy internships shall be conducted only in those hospitals in which the educational benefits to the intern are considered of paramount importance.

Guide to Hospital Qualifications

The director of the pharmacy internship program, the pharmacy staff, the director of interns and residencies in the hospital, and the hospital administrator should understand and agree to abide by the principle that the educational benefits to the pharmacy intern are of paramount importance, with the service benefits to the hospital of secondary significance and should be prepared to accept full responsibility for the proper training of the intern.

"A Manual for Pharmacy Internship in Hospitals"* is available for review by the program director for guidance in planning the total hospital pharmacy internship program.

III. Qualifications of Pharmacy Service

The pharmacy service shall comply with the requirements of the Minimum Standard for Pharmacies in Hospitals as approved by the Division of Hospital Pharmacy of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. In addition to the pharmacist-in-charge, there shall be at least one full time registered pharmacist for each full time intern.

The pharmacy shall comply in full with all federal, state and local laws, codes, statutes, and regulations, including Food and Drug and Public Health Laws and Regulations and State Hospital Licensing Act and regulations for pharmacy service in hospitals.

The pharmacy shall provide the following minimum activities or divisions of pharmacy practice:

A. Administration
B. Inpatient and general dispensing
C. Outpatient dispensing
D. Bulk compounding and preparation of sterile products
E. Bulk compounding and prepackaging of non-sterile products

Guide to Pharmacy Service

The chief pharmacist and his appointed assistant shall be active members of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. All other pharmacists on the staff should also hold active membership in these organizations.

If any of the designated activities or divisions of pharmacy practices are not available in the training hospital, arrangements shall be made with another hospital meeting the requirements of Section II of the Standard or with a facility acceptable to the Division of Hospital Pharmacy, to provide the necessary experience.

The director of the training program shall have completed a pharmacy internship in a hospital and have had two years of administrative experience in a hospital pharmacy, or have had at least five years experience in a pharmacy meeting the Minimum Standard for Pharmacies in Hospitals, part of which experience should have been of an administrative nature.

The pharmacy department should be adequately staffed with nonprofessional personnel so that the intern's time will not have to be routinely utilized in nonprofessional duties.

*Available from the Division of Hospital Pharmacy of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

IV. Qualifications of the Applicant

The applicant shall be a graduate of a school of pharmacy fully accredited by the American Council on Pharmaceutical Education.

Guide to Applicant Qualifications

The applicant shall have average or better recommendations from his college faculty and previous employers and shall have attained at least an average scholastic standing. The application shall include a statement of the applicant's personal background and pharmaceutical experience, and shall be accompanied by an official transcript of the applicant's pharmacy college record. Letters of recommendation shall be requested by the hospital from the dean and members of the faculty of the college of pharmacy and from the applicant's previous employers.

The American Council on Pharmaceutical Education shall be consulted concerning the acceptability of graduates of foreign schools or colleges of pharmacy.

V. Internship Schedule

Interns shall be assigned to and given supervised instruction in the following specific activities:

	Hours
A. Outpatient dispensing	250
B. Inpatient and general dispensing	320
C. Bulk compounding and preparation of sterile products	320
D. Bulk compounding and prepackaging of non-sterile products	320
E. Pharmacy administration	480
F. Collateral and interdepartmental special activities	185
G. Lectures and conferences	125
Total	2,000

Guide to Internship Schedule

Interns shall be assigned to and given supervised instruction in the specific activities outlined in Section V of the Standard.

In order that the intern may utilize his period of training in accordance with his specific needs, it is permissible to deviate up to a maximum of 20 percent

from the minimum hours assigned to a specific activity as long as the total training period is at least 2,000 hours.

An "Experience Record for Hospital Pharmacy Internship"* may be used as a guide for developing a record of activities included in the training program.

To broaden the scope of the pharmacy intern's training and experience, there should be planned visitations and work periods to other hospitals and hospital pharmacies, pertinent pharmaceutical and public health institutions, and manufacturing concerns.

The intern shall receive instruction and experience in the following basic divisions and activities:

A. Outpatient Dispensing

1. Scope of standard stock and its determination.
2. Preparation and maintenance of standard stock.
3. Labeling problems including patient directions and identifications.
4. Types of containers to be used for stock.
5. Permanency of individual items of stock and problems involved.
6. Maintenance of appearance of division and personnel.
7. Personnel attitudes and their effects on patients.
8. Outpatient relationships.
9. Pricing prescriptions and the problems involved with social service and clinical rate-downs for indigent patients. Relative community costs (medical) and competitive influences.
10. Relations and mutual problems encountered with community welfare agencies in the matter of supplying medical aid to indigent members of the community.
11. Control of stock by accounting procedures (inventory) and the control of revenue.
12. Problems presented by the extemporaneous prescription.
13. Policy concerning refilling of prescriptions.
14. Policy concerning drugs issued to hospital personnel.
15. Legal significance of the prescription—legal aspects and responsibilities including criminal and tort negligences.
16. Federal, state, county and city laws, codes, statutes and regulations affecting outpatient pharmacy service.

B. Inpatient and General Dispensing

1. Routine dispensing procedures.
2. Methods of preparation of stock for dispensing.
3. Labeling problems, including "floor stocks," coding, dating.
4. Storage and maintenance of adequate supplies.
5. Control of stock extended to hospital nursing floors and in clinical departments and the periodic inspection of medication stocks on these areas.
6. Problems entailed in extemporaneous prescription compounding.
7. The effect of the formulary system on pharmacy department.
8. Trends in drug therapy, types of illness, inpatient hospital census.
9. Accuracy in dispensing.
10. Critical analysis of written prescriptions—directions, dosage, quantity.
11. Federal, state, county and city laws, codes, statutes and regulations affecting inpatient pharmacy service.

C. & D. Bulk Compounding and Prepackaging of Non-Sterile and Sterile Products

1. Apparatus, its construction, operation and maintenance.
2. Bulk compounding and prepackaging of pharmaceuticals.
3. The preparation of supplies for dispensing, methods of filling containers and problems involved.
4. Storage of raw materials and completed preparations.
5. The preparation of injectible preparations.
6. Procedures for the sterilization of pharmaceuticals and equipment.
7. Control and assay procedures and maintenance of bulk manufacturing and prepackaging records.
8. The preparation of biological stains and reagents.
9. Bulk compounding of soaps, detergents, disinfectants and germicides.
10. Safety factors.
11. Factors to be considered in product formulation.
12. Prepackaging—purpose, scope, responsibilities, control procedures.
13. Surgical and central sterile supplies.

E. Administration

1. Organization plans for the pharmacy department.
2. Administrative policies.
3. Professional policies: (a) the formulary system and its application; (b) pharmacy and therapeutics committee—policies and procedures.
4. Personnel selection and management, staffing patterns for professional and nonprofessional personnel.
5. Supervision and its applications.
6. The licensing of pharmacists and pharmacies.
7. Control of narcotics, hypnotics, alcohol and other "legend" drugs.
8. Control of drug storage area in the hospital. Implications of non-control of dangerous drugs stored in centralized hospital store room.
9. Federal, state and local laws and their application (State Pharmacy, Food and Drug, Hospital Licensing Act, common law on criminal and tort negligence and contract law implications).

*Available from the Division of Hospital Pharmacy of the American Pharmaceutical Association and the American Society of Hospital Pharmacists.

10. Factors involved in supplying medical care to subscribers to a plan for comprehensive medical care insurance such as may be encountered in industry, government, trade union activities, or organized community plans.
11. Accounting procedures and inventory control.
12. Departmental budgeting.
13. Purchasing and/or requisitioning.
14. Library and reference sources.
15. Conduct in personal and telephone contacts with physicians, nurses and other professional people.
16. Departmental periodic reports of financial and professional activities.
17. Physical layouts and space requirements of hospital pharmacies.
18. Relations with other hospital departments.
19. Familiarity with the pharmacy elements of the Joint Commission on Accreditation of Hospitals and the forms used in the inspection procedure.
20. Safety practices.
21. Instruction (orientation) during the first week on hospital policies, rules and regulations for interns, attendance at indoctrination meeting with medical and dental interns.

F. Collateral and Interdepartmental Duties and Responsibilities of the Intern

1. Cooperation in teaching courses to students in the school of nursing and medical and dental intern programs.
2. The intern shall be encouraged to maintain membership and to participate actively in the functions of pharmaceutical, hospital and other professional associations. Attendance at a minimum of two pharmacy and therapeutics committee meetings shall be required of the pharmacy intern, at one meeting of which he shall serve as assistant secretary.
3. Clinical and therapeutic conferences conducted in the hospital shall be announced and the intern staff encouraged to attend if the subject matter is deemed pertinent.
4. A program of investigation covering some particular pharmaceutical problem shall be carried on during each intern service. The project may be selected from any of the activities in the intern program. In the academic program, research for credit in the graduate school may take the place of this investigation in the hospital pharmacy.
5. The intern shall be required to answer some emergency calls during hours when the pharmacy is closed.
6. The intern shall be encouraged to visit and observe procedures of operation in other nearby hospital pharmacies. In those areas where it is geographically and economically feasible, arrangements should be made between two or more institutions having approved internship programs for an exchange of interns for periods of from one week to one month.
7. The intern shall participate in conferences of the pharmacy department staff.
8. Rotation of the pharmacy intern through other departments of the hospital, such as internal medicine, surgery, obstetrics, pathology, radiology, clinical laboratory, bacteriology, nursing, dietetics, medical records, business and accounting offices. The intern shall participate in staff and committee discussions, seminars and demonstrations and work with interns from other services (medical, dental, etc.) on joint studies to become familiar with the professional and management activities that comprise the total hospital function with special reference to drug evaluation, selection, storage, utilization, control and drug research.

G. Lectures and Conferences

1. Lectures shall be conducted periodically by the pharmacist in charge or by one of his appointed assistants, covering the material included in the "Syllabus for a Course in Hospital Pharmacy." These lectures shall consider the theoretical aspects of the problems concerned with each subdivision as well as hospital pharmacy administration and interdepartmental relations. The pharmacist in charge shall arrange for the hospital administrator and other department heads to participate in the lectures. In lieu of these lectures, a formal course in hospital pharmacy administration may be taken by the intern in the academic program.
2. Conference periods, such as journal clubs, shall be conducted to review current and past literature and recent developments in the fields of pharmacy, medicine, pharmacology, biochemistry, microbiology, hospital practices, and other related subjects as they pertain to hospital pharmacy practice.
3. Upon completion of training in each specific activity, a conference should be held with the intern to review the theoretical and practical aspects of that particular activity.

VI. Certification

An appropriate certificate indicative of successful completion of the prescribed internship shall be awarded to the intern by the hospital.

The hospital shall be awarded an appropriate certificate by the Division of Hospital Pharmacy of the American Pharmaceutical Association and the American Society of Hospital Pharmacists testifying to the fact that it is approved for offering internship in hospital pharmacy.

Guide to Certification

The certificate, which is awarded to the hospital certifying approval of its pharmacy internship, shall be the property of the Division of Hospital Pharmacy and may be removed for cause.

The Division of Hospital Pharmacy shall submit annually full information on Approved Internship Programs in Hospital Pharmacy to the American Journal of Hospital Pharmacists and to hospital association and medical journals for publication in the appropriate annual issues.

Statement of Principles Involved in the Use of Investigational Drugs in Hospitals

Approved by Board of Trustees of the American Hospital Association, September 29, 1957

► HOSPITALS ARE THE PRIMARY CENTERS for clinical investigations on new drugs. By definition these are drugs which have not yet been released by the Federal Food and Drug Administration for general use.

Since investigational drugs have not been certified as being for general use and have not been cleared for sale in interstate commerce by the Federal Food and Drug Administration, hospitals and their medical staffs have an obligation to their patients to see that proper procedures for their use are established.

Procedures for the control of investigational drugs should be based upon the following principles:

1. Investigational drugs should be used only under the direct supervision of the principal investigator who should be a member of the medical staff and who should assume the burden of securing the necessary consent.

2. The hospital should do all in its power to foster research consistent with adequate safeguard for the patient.

3. When nurses are called upon to administer investigational drugs, they should have available to them basic information concerning such drugs — including dosage forms, strengths available, actions and uses, side effects, and symptoms of toxicity, etc.

4. The hospital should establish, preferably through the pharmacy and therapeutics committee, a central unit where essential information on investigational drugs is maintained and whence it may be made available to authorized personnel.

5. The pharmacy department is the appropriate area for the storage of investigational drugs, as it is for all other drugs. This will also provide for the proper labeling and dispensing in accord with the investigator's written orders.

Report: Committee on Hospital Pharmacy Education

of the American Association of Colleges of Pharmacy

presented by TOM ROWE, *Chairman*

► THE COMMITTEE MET in Columbus, Ohio, on January 18, 1957 with all members present. The following day we met jointly with the Committee on Curriculum and presented our recommendations and conclusions to them.

Prior to the Columbus meeting, the Committee on Hospital Pharmacy Education had carried on considerable correspondence and had agreed on several major problems for study. We decided at the meeting to concentrate this year on proposals for an undergraduate program in hospital pharmacy, and our work was directed toward this end. Plans for next year call for consideration of the graduate program. Note should be taken that the program described in this report is a modest start at the undergraduate level towards specialized training in hospital pharmacy. It is supplementary to current and planned graduate programs in this area and should serve to strengthen and help extend them.

We agreed that all courses required in the five year program for retail pharmacy are probably needed for every field of pharmacy and certainly for hospital pharmacy. We decided, therefore, to suggest work beyond the required courses which would help qualify students to enter the field of hospital pharmacy. We assumed there would be provision for professional electives in the last two years of the five-year curriculum and that courses suggested by us could be taken as professional electives.

After discussing at least eight courses for inclusion in this area, we selected three we considered to be essential for a minimum exposure to hospital pharmacy.

1. Manufacturing Pharmacy—3 credit hours per semester, 2 semesters

2. Hospital Pharmacy Management—2 credit hours 1 semester

3. Hospital Pharmacy Seminar—2 credit hours, 1 semester

These courses total ten semester credit hours. This is actually only eight more than was suggested by the Curriculum Committee inasmuch as they already provide for two credit hours in Manufacturing Pharmacy. These courses are described in this report without attempting to outline a complete syllabus.

Members of the Committee on Hospital Pharmacy Education of the A.A.C.P. included TOM ROWE, Chairman, WILLIAM E. HASSAN JR., WILLIAM E. HELLER, DONALD H. SKAUEN, and JOHN J. ZUGICH.

Manufacturing Pharmacy. Material described in Blauch and Webster* under Manufacturing Pharmacy should be included, but individuals planning to go into hospital pharmacy need more detailed coverage than is provided for in the single, two-hour course. While it is not our intent to list the order or the amount of time to be devoted to each topic, we feel that considerable emphasis should be placed on sterile preparations such as fluids packaged in both large and small containers, ophthalmic solutions, and allergenic extracts. In some instances the college may plan to organize a separate course in sterile manufacturing or parenteral preparations. We believe this area is of especial importance in hospital pharmacy.

In addition to the preparation of dosage forms in large quantities, which would be included in any manufacturing pharmacy course, we felt that there should be some time spent on laboratory reagents whose preparation is so frequently the responsibility of the hospital pharmacy. It is assumed, of course, that in manufacturing pharmacy, control will be emphasized so that a hospital pharmacist, by applying his knowledge from other courses, will insure provision of adequate control procedures for preparations manufactured in the hospital pharmacy.

Hospital Pharmacy Management. This course is usually designated Hospital Pharmacy Administration. The term "management" in place of "administration" is more accurately descriptive of the course. Inasmuch as the title Hospital Pharmacy Administration is already widely used, however, the course will probably be continued to be taught under this name. The syllabus suggested in the May-June, 1955 issue of *The Bulletin of The American Society of Hospital Pharmacists* can be used as a guide here. Therein some lectures are suggested dealing with techniques in manufacturing. This work should not be duplicated and the course in Management should not concern itself with techniques. Careful correlation between this course and the one in Manufacturing Pharmacy is indicated.

We feel that wherever possible, hospitals should be used as "laboratories" to illustrate the material presented in this course. If the undergraduate students are given experience in hospital pharmacies, they will be much better prepared to solve problems in this area when they start practice on their own.

Hospital Pharmacy Seminar. The term "seminar" describes essentially what this course should be. There is some question about the use of "seminar" for an undergraduate course, but we are informed that this is common practice in a number of schools today. In the Seminar, papers based on library research would be presented by the students. General problems related to hospital pharmacy would also be discussed. The objective of the Seminar would be to give as broad a picture of the actual operation of a hospital pharmacy as is possible.

While these courses constitute more than an introduction to the field, the Committee believes they would give reasonably adequate preparation for practice in a hospital pharmacy; certainly better preparation than the required courses only of the usual retail pharmacy curriculum.

For the Management and the Seminar courses, teachers should be pharmacists who have had, or are currently engaged in, practice in hospitals meeting the minimum standards of the American Society of Hospital Pharmacists.

The three courses suggested are included in most of the hospital pharmacy programs leading to a Master of Science. It is our belief that all three subjects could be offered to both graduates and undergraduates, particularly if elected by the undergraduates in their senior year. Students who undertook graduate study in hospital pharmacy should be given an advanced course in Hospital Pharmacy Management.

The courses recommended could all be given during the senior undergraduate year with Manufacturing Pharmacy given concurrently with the other two courses. Hospital Pharmacy Management should precede the Seminar course. If it is necessary to give at least one of these subjects in the junior undergraduate year, then this should be Manufacturing Pharmacy.

In addition to the courses recommended, we discussed three other areas which we feel are of importance to all pharmacy students and particularly to those entering hospital pharmacy. One of these is a course in Public Health. This course is taught in many schools and is recommended as required by Blauch and Webster. However, their figures show that only slightly more than one half of the schools now offer this subject. We feel it is of particular importance to the hospital pharmacist. They of all pharmacists should be keenly aware of the position of pharmacy in relation to the other health sciences. Schools not now offering this course should certainly find it possible to do so in the five-year program.

We had planned to suggest a required course in dispensing using radio-active isotopes. This course should include laboratory work, and the number of schools in which it can be taught will be limited. We do not, therefore, recommend it as a required subject. We strongly urge all schools having facilities for laboratory instruction in this field to offer such a course.

The last point we felt to be of considerable importance does not necessarily involve offering a separate course. It concerns terminology. It is our feeling, and we believe it is generally shared by most pharmacy teachers, pharmacy graduates are not as well equipped in this area as they should be. They are not able to understand many of the common medical terms and are at a disadvantage when talking to a physician. This is particularly noticeable to hospital pharmacists themselves, and they agree that they should be better versed in medical terminology. We believe introduction to the derivation of words should come early in the professional curriculum and the use of medical terms should be stressed throughout all of the courses. Inasmuch as this defect is of general interest and not limited to hospital pharmacy, we felt action on this problem was not a specific responsibility of this Committee. We would like to direct attention of the Curriculum Committee to the problem and recommend study leading to a solution helpful to all pharmacy students.

The Committee on Hospital Pharmacy Education believes that the courses in hospital pharmacy suggested in this report will help appreciably in meeting the critical manpower shortage in this field. We recognize that the number of students receiving Master of Science degrees with a major in hospital pharmacy is far too small to meet the current needs, and that graduate programs in hospital pharmacy will not be able to meet the demands in the forseeable future.

We hope, therefore, that by following the suggestions made in this report, there will be more students interested and better qualified than now to enter into the field of hospital pharmacy. We also hope that having been introduced to it on an undergraduate level, more students will elect to go on for graduate work.

We wish to thank Dean Parks for the fine arrangements he made for us while we were in Columbus and for the courtesies he extended to our Committee.

* The Pharmaceutical Curriculum, by Lloyd E. Blauch and George L. Webster. Published by the American Council on Education, Washington, D. C. 1952

MY HOBBY

—collecting antique mortars

by JOSEPH S. BARRY

► This hobby of collecting antique mortars and pestles began in 1940 when the president of a medical supply company brought an old mortar and pestle to place on my desk. I decided then and there I would start a collection of them and any other article which was used by the retail pharmacist of years gone by.

Once started, many mortars and pestles were given to me by friends who found out I was collecting them. Even patients who came by the Pharmacy and saw them on display have presented some to me.

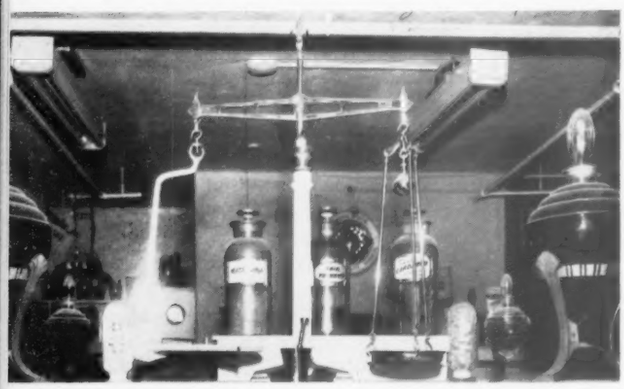
I have about two hundred mortars and pestles running all the way from stone, wood, brass, iron and wedgewood. The stone one, about three hundred years old, is located about the center of the photograph, immediately to the left below my registration certificate. The mortar and pestle immediately under my registration certificate were given to me by a friend who worked in the hospital. It is of solid mahogany and weighs over 20 pounds and had been a family treasure for years and years. A brass one was found in the rubble on the Wilhemstrasse in Germany in a bombed out physician's office building and sent to me by one of our nurses during the war. Another of Lignum Vita was shipped to me from Haiti by one of our dental officers. Another, the fourth to the right on the shelf second from the top, comes from Sweden and it has the following inscription on the bottom written in ink "From the wooden wedding Dec. 26, 1876. Mrs. Sarah Pond." The one I hold in my hand was shipped to me from Sweden last year by an employee on vacation. Most of them, however, were picked up in antique shops around New England. One salesman who knew I collect mortars and pestles brought in ten in one lot. He had obtained them in Maine. As I go around now I find they are getting scarce and the price of some of them is prohibitive.

Besides the mortars and pestles, I also have a fine collection of hand blown tincture and salt mouth bottles with real old gold labels. About fifty of them are blue glass with gold labels. Also I have several scales. I also have a small and complete konseal machine and many other items which are too numerous to mention.

The prize one, though, is a box of laxative pills which reads on one side of the box "Will cure appendicitis if taken in time." This is from a collection of old patent medicines before the Pure Food and Drug Act was enacted.

Antique mortars and pestles displayed in Mr. Barry's office

Below: An unusual set of scales



JOSEPH S. BARRY is Chief Pharmacist at The Memorial Hospital, Worcester, Mass.

Joseph Barry shown with part of his collection of antique mortars

Therapeutic Trends

edited by WILLIAM JOHNSON

Anisindione—Anticoagulant Properties

Anisindione (2-p-anisyl indandione-1,3) is an anticoagulant of the indandione type. It was given to 52 patients with vascular disease, but not always the thromboembolic type, for a total of 1,198 days. A dosage schedule was worked out which started with an initial dose of 500 mg. the first day, 300 mg. the second day, nothing on the third day, and 300 mg. the fourth day. The maintenance dose (in most cases) was found to be 250 mg. Anisindione every third day. Initial rapid fall in prothrombin activity is observed which reaches a therapeutic level within 36 to 72 hours. The effect of the drug can be rapidly interrupted by the use of phytonadione. The anticoagulant effect can be restored rapidly by remedication. Maintenance doses of the drug retain the anticoagulant effect previously established with Dicumarol. There was no chromaturia, petechiae, agranulocytosis, or liver damage observed in this group. This study by Lange *et al* is reported in *Am. Heart J. 55*:73 (Jan.) 1958.

Deanol—A Cerebral Stimulant

In a series of over 100 patients suffering from various psychiatric disorders, especially exhaustion and depression, the clinical effect of Deanol was studied by Lemere and Lasater as reported in *Am. J. Psychiat. 114*:655 (Jan.) 1958. Deanol (para-acetylaminobenzoate) is a precursor of acetylcholine which is essential to the transmission of impulses between neurons. Clinical effects observed were increased energy and lessened depression in the majority of cases. Dosage ranges from 10 to 50 mg. given as a single daily oral dose after breakfast. The only side effect observed was overstimulation in a few cases which was controlled by a reduction in dosage. There was no indication of dependency or tolerance to the drug. In this series, approximately 70 percent of the patients expressed a preference for this medication over other drugs previously used. Deanol does not seem to be effective in cases of severe depression especially those with agitation. Deonal was supplied for the study by Riker Laboratoriees.

SC-6584—A Hypotensive Steroid

SC-6584 (17 a-propyl-4,5b-dihydro-19-nortestosterone) significantly lowered the blood pressure of metacorticoid, metarenal and adrenal-regeneration hypertensive rats in acute and chronic studies. The compound displayed no appreciable activity in the following types of assays: anabolic, androgenic, estrogenic, lipodiatic, progestational, glucocorticoid, antiphlogistic, eosinopenic, antiarrhythmic, and anesthetic. However, SC-6584 potentiated barbiturate anesthesia. In none of the experiments reported was any toxic effect of SC-6584 noted. This report describing the pharmacologic properties of SC-6584 is presented by Sturtevant in *J. Pharmacol. Exptl. Ther. 121*:369 (Nov.) 1957.

Amicetin B—An Antibiotic

In the course of a systematic screening for a new antibiotic-producing streptomycetes, a new strain designated as *Streptomyces 285* and isolated from a soil sample of the Parque Forestal of Santiago de Chile was found to produce in submerged, aerated culture, antibiotic activity against gram-positive bacteria and mycobacteria. The chemical and physical properties and the study of the degradation products after acid and alkaline hydrolysis show that the new antibiotic is similar to amicetin, the only difference consisting of the absence of the amino acid, dextro-a-methylserine, in its molecule. The antibiotic has been therefore designated as amicetin B. It is poorly soluble in water and the usual organic solvents. It is basic in character, giving salts with organic and inorganic acids. This study is reported by Sensi *et al* in *Antibiot. and Chemother. 7*:645 (Dec.) 1957.

Synnematin B—Treponemicidal Agent

The treatment of a case of primary syphilis with synnematin B is reported by Wheeler *et al* in *Arch. Dermatol. 76*:735 (Dec.) 1957. An initial dose of one million units of synnematin B was given intramuscularly. Twenty-four hours later no spirochetes were observed in dark-field examination of material from either the chancre or the inguinal nodes. The patient was hospitalized to facilitate multiple administrations of the drug and clinical and laboratory examinations. While in the hospital the patient received 40,000 units of synnematin B, intramuscularly, three times daily for eight days. Seven months after discharge, the patient was re-examined and showed no clinical evidence of syphilis.

Timely Drugs

Butazolidin Alka

COMPOSITION: Phenylbutazone (Butazolidin), aluminum hydroxide, magnesium trisilicate, and homatropine methylbromide.
INDICATIONS: Anti-arthritic with antacid-antispasmodic components.
DOSAGE: As directed by physician.
PREPARATIONS: Capsules containing phenylbutazone 100 mg., aluminum hydroxide 100 mg., magnesium trisilicate 150 mg., and homatropine methylbromide 1.25 mg.
PACKAGING: Bottles of 100 capsules.
SUPPLIER: Geigy Pharmaceuticals.

Chymar Aqueous

CHEMICAL NAME: Chymotrypsin.
INDICATIONS: Systemic anti-inflammatory agent, to reduce and prevent inflammation, edema and pain, blood extravasates and lymph effusions in accidental injuries, surgery, obstetrics, eye diseases and oral surgery; as adjunctive with antibiotics in treatment of infected wounds; and in prophylaxis of lesions prone to infection.
DOSAGE: 0.5 to 1 ml. intramuscularly 1 to 3 times daily until clinical improvement is obtained; in chronic or recurrent inflammation, 0.5 to 1 ml. once or twice weekly.
PREPARATIONS: Crystallized chymotrypsin 5,000 Armour units per ml. in sodium chloride injection.
PACKAGING: 5 ml. vials.
SUPPLIER: Armour Laboratories.

Cosa-Tetracyn

COMPOSITION: Tetracycline hydrochloride and glucosamine.
INDICATIONS: Antibiosis; higher blood levels attained with glucosamine, a non-toxic naturally occurring substance in human tissue, secretions and organs.
SIDE EFFECTS AND CONTRAINDICATIONS: Possible overgrowth of non-susceptible organisms as with other antibiotics.
DOSAGE: Adults, 1 Gm. divided into 4 equal parts; children's dosage proportionately less.
PREPARATIONS: Capsules of 125 mg. and 250 mg.
PACKAGING: Bottles of 25 and 100 of 125 mg. capsule, and of 16 and 100 of 250 mg. capsule.
SUPPLIER: Pfizer Laboratories.

Cyclamycin

CHEMICAL NAME: Triacetyloleandomycin.
INDICATIONS: Antibiotic effective against some gram-negative and most gram-positive organisms.
SIDE EFFECTS AND CONTRAINDICATIONS: Overgrowth of non-susceptible organisms, particularly monilia, may occur with continued use.
DOSAGE: Orally, in adults, 250 to 500 mg. four times daily; children 8 to 15 years, 125 mg. to 250 mg. four times daily; children up to 8 years, 20 to 40 mg. per Kg. body weight daily in divided doses. Intravenously, for adults, 1 to 2 Gm. daily in equally divided doses every 6 to 12 hours; infants and children, 40 mg. per Kg. body weight daily.
PREPARATIONS: Capsules 125 mg. and 250 mg.; oral suspension containing 125 mg. per 5 ml.; injection, phosphate salt, dry powder, vials containing 500 mg.
PACKAGING: Capsules, bottles of 36; oral suspension, bottles of 60 ml.
SUPPLIER: Wyeth Laboratories.

Deprol

COMPOSITION: Meprobamate and benactyzine hydrochloride.
INDICATIONS: Ataraxic, counteracts depressed moods without stimulation or euphoria, restores natural sleep without depressive after effects.
DOSAGE: One tablet 4 times daily.
PREPARATIONS: Tablets containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.
PACKAGING: Bottles of 50 tablets.
SUPPLIER: Wallace Laboratories.

Erythrocin—I.M.

GENERIC NAME: Erythromycin ethyl succinate.
INDICATIONS: Infections caused by organisms sensitive to erythromycin, including most of the gram-positive cocci.
SIDE EFFECTS AND CONTRAINDICATIONS: *Must not be administered intravenously or subcutaneously.*
DOSAGE: Adults, 100 mg. every 6 hours; children, dosage reduced in proportion to age and weight.
PREPARATIONS: Sterile solution in polyethylene glycol containing 50 mg. per ml.
PACKAGING: 2 ml. ampuls and 10 ml. vials.
SUPPLIER: Abbott Laboratories.

Gastrografin

COMPOSITION: Sodium and methylglucamine diatrizoates (Renografin).
INDICATIONS: Radiopaque medium to be administered orally, by tube or by rectum, for roentgenographic study of gastrointestinal tract.
SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally diarrhea and, rarely, nausea and vomiting; contraindicated in iodine sensitivity.
DOSAGE: Orally, 30 to 90 ml. depending on nature of examination and size of patient; may be diluted to 50 percent with water, milk, mineral oil or carbonated beverages; higher dilutions may be used for enemas and enterostomy instillations, and in infants; may be administered to infants in nursing bottle.
PREPARATIONS: Aqueous, lemon-flavored solution containing Polysorbate 80 U.S.P. and an antifoaming agent to aid dispersion into mucosal folds.
PACKAGING: Bottles of 120 ml.
SUPPLIER: E. R. Squibb & Sons.

Kenacort

CHEMICAL NAME: Triamcinolone (9-alpha-fluoro-16-alpha-hydroxy derivative of prednisolone).
INDICATIONS: Anti-inflammatory and antiallergic corticosteroid therapy in arthritic disorders and allergy disorders.
SIDE EFFECTS AND CONTRAINDICATIONS: Usual signs of

cortisone overdosage do not apply, thus careful observance of patient is necessary; contraindicated in active tuberculosis or acute or chronic bacterial infections unless infection is controlled with appropriate antibiotic or chemotherapeutic means.

DOSAGE: Generally, one-third less than that of prednisolone.

PREPARATIONS: Tablets containing 1 mg. and 4 mg.

PACKAGING: Tablets of 1 mg., bottles of 50 and 500; tablets of 4 mg., bottles of 30, 100 and 500.

SUPPLIER: E. R. Squibb & Sons.

Mumps Immune Globulin (Human)

COMPOSITION: Gamma globulin fraction of blood from healthy, adult, human donors who have been hyperimmunized with mumps virus vaccine.

INDICATIONS: Passive prevention and treatment of mumps in children and adults.

DOSAGE: For prophylaxis, 1.5 ml. for children up to 90 pounds, 3 ml. between 90 and 140 pounds, 4.5 ml. over 140 pounds; for treatment, either larger dose or repeated after 24 to 48 hours, with further dosage if parotitis reappears or fails to disappear.

PREPARATIONS: A 16.5 percent solution; each 1.5 ml. is equivalent in antibody content to at least 30 ml. original hyperimmune serum.

PACKAGING: 1.5 and 4.5 ml. vials.

SUPPLIER: Hyland Laboratories.

Mycifradin—N

COMPOSITION: Neomycin (Mycifradin) sulfate and nystatin.

INDICATIONS: Preoperative preparation of bowel prior to abdominal and/or perineal surgery involving lower intestinal tract.

SIDE EFFECTS AND CONTRAINDICATIONS: Intestinal obstruction.

DOSAGE: After saline cathartic, 2 tablets; repeat every 4 hours for total of 12 tablets.

PREPARATIONS: Compressed tablets containing neomycin sulfate 0.5 Gm. and nystatin 125,000 units.

PACKAGING: Bottles of 20, 100, and 500 tablets.

SUPPLIER: Upjohn Co.

Sudafed

CHEMICAL NAME: Pseudoephedrine hydrochloride.

INDICATIONS: Nasal decongestant, with simultaneous bronchodilating action.

DOSAGE: Older children and adults—60 mg. 3 or 4 times daily; children 4 months to 6 years—30 mg. 3 or 4 times daily; infants up to 3 months of age—15 mg. 3 or 4 times daily.

PREPARATIONS: 30 ml. sugar-coated tablets and 60 mg. scored, uncoated tablets.

PACKAGING: Bottles of 100 tablets.

SUPPLIER: Burroughs Wellcome & Co.

Ultra-Lente Iletin

COMPOSITION: Crystalline suspension of modified insulin (Iletin).

INDICATIONS: For controlled duration of action in diabetes; duration of effect is about 36 hours or more.

SIDE EFFECTS AND CONTRAINDICATIONS: Not recommended in the treatment of diabetic emergencies such as diabetic coma.

DOSAGE: Individually determined.

PREPARATIONS: U-40 and U-80 containing respectively 40 units and 80 units per ml., in 10 ml. vials.

SUPPLIER: Eli Lilly & Co.

Panalba KM Flavored Granules

COMPOSITION: Tetracycline (Panmycin), novobiocin (Albamycin) calcium, and potassium metaphosphate.

INDICATION: Same as for other tetracycline products.

DOSAGE: For moderately acute infections in infants and children, 5 ml. per 15 to 20 pounds body weight daily in 2 to 4 equally divided doses; for adults, 5 to 10 ml., 3 or 4 times daily.

PREPARATIONS: Dry granules, when diluted to 60 ml., containing in each 5 ml., tetracycline equivalent to the hydrochloride 125 mg., novobiocin calcium 62.5 mg., and potassium metaphosphate 100 mg.

PACKAGING: 60 ml. bottles, to be diluted with 48 ml. water.

SUPPLIER: Upjohn Co.

Pediagesic

COMPOSITION: Acetaminophen (Metalid) and salicylamide (Salamide).

INDICATIONS: Analgesic and antipyretic, especially designed for pediatric use.

DOSAGE: Infants, ½ teaspoonful every 4 to 6 hours; children 1 to 4 years, ½ to 1 teaspoonful every 4 to 6 hours; children 4 to 6 years, 1 to 2 teaspoonfuls every 4 to 6 hours; over six years, 2 teaspoonfuls every 4 to 6 hours.

PREPARATIONS: Orange or lime-flavored medication containing in each teaspoonful acetaminophen 60 mg. and salicylamide 60 mg.

PACKAGING: Bottles of 3 ounce.

SUPPLIER: Columbus Pharmacal Co.

Pertussis Immune Globulin (Human)

COMPOSITION: Gamma globulin fraction of blood from healthy, adult, human donors who have been hyperimmunized with pertussis vaccine (phase I).

INDICATIONS: Passive prevention and treatment of whooping cough.

DOSAGE: Intramuscularly, for prophylaxis, 1.5 ml. as soon as possible after exposure; second 1.5 ml. dose, week after first, is desirable; repeat dosage at 1 to 2 week intervals if exposure continues. Intramuscularly, for treatment, 1.5 ml. when symptoms appear; additional doses at 1 to 2 day intervals until recovery has begun; for critically ill children, initial dose may be doubled.

PREPARATIONS: A 16.5 percent solution; each 1.5 ml. is equivalent in antibody content to at least 25 ml. original hyperimmune serum.

PACKAGING: 1.5 ml. vials.

SUPPLIER: Hyland Laboratories.

Semi-Lente Iletin

COMPOSITION: Suspension of amorphous modified insulin (Iletin).

INDICATIONS: For controlled duration of action in diabetes; duration of effect is about 12 to 16 or 18 hours.

SIDE EFFECTS AND CONTRAINDICATIONS: Not recommended in the treatment of diabetic emergencies such as diabetic coma.

DOSAGE: Individually determined.

PREPARATIONS: U-40 and U-80 containing respectively 40 units and 80 units per ml., in 10 ml. vials.

SUPPLIER: Eli Lilly & Co.

Notes & Suggestions

edited by CLIFTON J. LATIOLAIS

SULFAETHYLTHIADIAZOLE INJECTION 25%

Sulfaethylthiadiazole (American Cyanamid)	25.0 Gm.
Diethanolamine (Carbide and Carbon)	9.5 ml.
Freshly distilled water, to make	100.0 ml.

Dissolve ingredients in the water, filter through a fine porosity sintered glass filter, fill into 10 ml. ampuls, and autoclave. *p*H—7.5-8.1 (*J. Am. Pharm. Assoc. Sci. Ed. 46*:404 (July) 1957.)

LUBRICATING JELLY

A new lubricating jelly is described by Levy and and Schwarz in the November 1957 issue of *Drug and Cosmetic Industry* (page 606). This jelly contains synthetic ingredients rather than natural gums. It is heat stable and can be autoclaved without affecting the viscosity. It is stable on storage, transparent, and bacteriostatic. In addition, it has a higher yield strength than other jellies and therefore does not drip. Since the total solid content is only 1.5 percent the formation of a residual film after application is minimized.

*Methocel 90 HG 4000	1.0 Gm.
**Carbopol 934	0.3 Gm.
Sodium hydroxide solution 1% to make *p*H of	7.0 (about 12 ml.)
Propylene glycol USP	20.0 ml.
Methylparaben USP	0.15 Gm.
Propylparaben USP	0.05 Gm.
Distilled water, to make	100.0 ml.

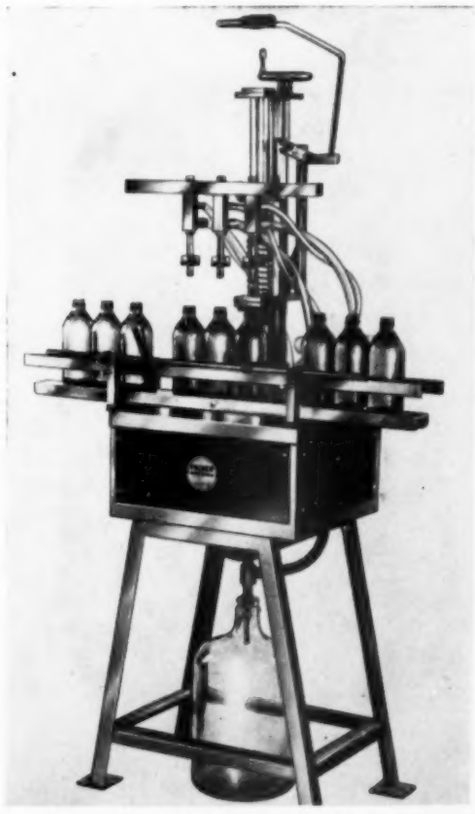
Slowly add the methocel to 40 ml. of hot water (80-90° C.) and rapidly agitate for about five minutes. Cool and store the solution in a refrigerator overnight. Dissolve the Carbopol in 20 ml. of distilled water by rapid agitation. Let stand until air bubbles dissipate and then add a 1 percent solution of sodium hydroxide slowly until a *p*H of 7.0 is obtained. Then add enough water to make 40 ml. Dissolve the parabens in the propylene glycol. Then mix the methocel, Carbopol, and paraben solutions together and stir slowly.

*Dow Chemical Company, Midland, Michigan. (brand of hydroxypropylmethylcellulose)

**B. F. Goodrich Chemical Company (brand of high molecular weight carboxylic polymer)

BOTTLE FILLER, VACUUM

The Model A is the smallest model in the Packer* line of straightline, semi-automatic liquid fillers. Ease of installation and operation makes this machine a desirable production unit. Available in three-spout assemblies, the unit is designed to carry up to six spouts, enabling one to increase production merely by purchasing additional spouts.



The vacuum model fills directly from a drum, tank, carboy, or other type container resting on the floor. Containers are accurately filled to any predetermined level; an attachment handles the overflow of liquid. The machine fills containers from fractional ounces to quarts. Dimensions are 36″ wide x 20″ deep x 64″ high. Height of filling rail is 35½″. The approximate price for the Model A vacuum filler is $655.

*Packer Machinery Corp. 109-14th St., Brooklyn 15, New York

DRUG REFRIGERATOR CATALOG

An illustrated, 20-page booklet on commercial refrigerators is available from Victory Metal Manufacturing Corporation, Plymouth Meeting, Pa. Among the 151 refrigerators of various sizes and types are models which are particularly adaptable for the storage of pharmaceutical and biological products in the hospital pharmacy. These refrigerators are offered in stainless steel, aluminum, or white baked enamel construction.

ULTRAVIOLET LIGHTED STORAGE TANK

The Barnstead Still and Sterilizer Company announces a new distilled water storage tank designed with built-in ultraviolet light for the continuous sterilization of contents. The ultraviolet light is set at a special frequency and is mounted above the surface of the water.

The problem of producing and storing distilled water and sterile solutions has plagued technicians ever since the presence of bacteria has been identified as a problem. At the moment, essentially all of the solutions made up as a sterile end product, must be autoclaved after final bottling, excepting those solutions that cannot stand heat sterilization. By using the Barnstead ultraviolet storage tank coupled with other Barnstead protection devices such as the Barnstead Ventgard, and the Barnstead Millipore Filter, sterility of contents can be maintained and in many cases final sterilization steps eliminated.

Barnstead ultraviolet tanks may be supplied in capacities from 5 to 1,000 gallons including vertical cylindrical, and box-type tanks. Further information may be obtained from Barnstead Still and Sterilizer Company, Lanesville Terrace, Boston 31, Massachusetts.

SCOOP-FUNNEL

The single styrene scoop-funnel S-1366X* can be used with either granulated material or liquids. (Powdered material tends to pack and will not pass through the funnel aperture.) Designed for filling small neck bottles and vials, the thumb regulates the flow of material which can be cut off instantly. Costs $0.69 each or $7.92 per dozen.

*Scientific Glass Apparatus Company, Inc., Bloomfield, N.J.

PAPAIN ENEMA

In the August 1957 issue of the U. S. *Armed Forces Medical Journal* (p. 1131) Godfrey and Miller report on the effectiveness of papain solution as an enema in the treatment of fecal impaction. Of the 14 different substances used in clinical trials, the investigators concluded that papain was the most effective agent. The formula used was:

Papain, crystalline 0.13 Gm. (or 5 Gm. of Caroid* powder)
Benzalkonium chloride solution 1:5000 to make 300.0 ml.

*American Ferment Company, Inc., New York, New York.

PIPERAZINE CITRATE ELIXIR, B.P.C.*

Piperazine citrate	180.0 Gm.
Peppermint spirit	5.0 ml.
Glycerin	100.0 ml.
Solution of Sulphan Blue with Tartrazine	15.0 ml.
Syrup	500.0 ml.
Water, to make	1000.0 ml.

Dissolve the piperazine citrate in part of the water, add the solution of Sulphan Blue with tartrazine, glycerin, syrup, peppermint spirit and sufficient water to produce the required volume.

Note: Solution of Sulphan Blue with tartrazine may be prepared as follows: Sulphan Blue 3.0 Gm., tartrazine 3.0 Gm., chloroform water to make 1000 ml.

*British Pharmaceutical Codex, Supplement 1957, page 94.

ISOPRENALINE SULFATE SPRAY, B.P.C.*

Isoprenaline sulfate	10.0 Gm.
Propylene glycol	50.0 ml.
Sodium metabisulfite	1.0 Gm.
Distilled water, to make	1000.0 ml.

Dissolve.

*British Pharmaceutical Codex 1954, page 1142.

Consulting WITH BOWLES

GROVER C. BOWLES JR., *Baptist Memorial Hospital, Memphis, Tennessee*

► What is the prevailing salary for hospital pharmacists in the Mid-West?

So far as I know, there is no such thing as a prevailing salary for hospital pharmacists. Salary is a very personal thing and is something that must be determined by your ability, your experience, the job you have to do, the number of pharmacists available to do the job, the administrator's opinion of hospital pharmacy, the salary of other department heads within the hospital family, and the hospital's ability to pay. Available fringe benefits such as life insurance, hospitalization insurance, retirement plan, sick leave, and vacation also must be considered when arriving at a reasonable salary. I have no specific information about salaries paid to hospital pharmacists in the Mid-West and I do not believe that you will find a "prevailing" or an "average" salary.

► Is the reuse of disposable plastic tubing considered safe?

The following information is quoted from the *Journal of the American Medical Association,* Volume 163, No. 13, pp. 1197, 1957.

"Although sufficient information is not available on this subject to permit a categorical answer to the question, it can be stated that on the basis of the information now available it is not believed that it would be feasible or advisable to reuse disposable plastic tubing for intravenous or subcutaneous fluid administration. The types of plastic tubing now available might not withstand the high temperatures necessary to assure destruction of bacterial spores and the virus responsible for infectious hepatitis. In this connection the following information from the book "Principles and Methods of Sterilization," by John J. Perkins (Springfield, Ill., Charles C. Thomas, Publisher, 1956), may be of interest:

The National Institutes of Health stipulate that apparatus and instruments capable of transmitting serum hepatitis from one person to another be heat-sterilized with minimum requirements as follows: "Heat sterilization shall be by autoclaving for 30 minutes at 121.5°C (15 lb. pressure), by dry heat for 2 hours at 170°C., or by boiling in water for 30 minutes." Since the thermal resistance of the virus appears to be equal that of bacterial spores it would seem unwise to attempt sterilization by any means other than the most reliable methods.

Another article of possible interest in connection with the subject of this inquiry is that of Randall B. Tinker, published in *The Bulletin of the American Society of Hospital Pharmacists,* July-August, 1956, page 319, under the title "A Case for Disposable Hypodermic Needles."

► Who is responsible for appointing the Pharmacy and Therapeutics Committee?

The Pharmacy and Therapeutics Committee is a standing committee of the medical staff and is ordinarily appointed by the chief of the medical staff. However, the hospital pharmacist and the hospital administrator are in a good position to stimulate interest in the formation and development of the committee.

► There is much confusion among the physicians on our staff about automatic stop orders. What, specifically does the Joint Commission on Accreditation of Hospitals expect in the way of automatic stop orders?

This question is best answered by quoting directly from the December 1957 issue of the Joint Commission on Accreditation of Hospitals *Bulletin* which lists the standards for the Pharmacy Department.

The JCAH standard simply states: "There shall be an automatic stop order on dangerous drugs."

Further elaboration by the Joint Commission contained in the same *Bulletin* will eliminate much of the confusion existing about automatic stop orders. "The requirement of an automatic stop-order on dangerous drugs is misunderstood frequently by hospitals and physicians. The Joint Commission on Accreditation of Hospitals has no right to tell physicians what kind and how much medicine they should give to their patients, and does not do so. The Commission does desire that drugs, especially dangerous drugs, be given properly with reasonable medical staff controls. The Commission is asking that hospital medical staffs establish a written policy that all dangerous medications, not specifically prescribed as to time and number of doses, be automatically stopped after a reasonable time limit set by the staff. It is a protection against indiscriminate, indefinite prescribing of an open-ended type which can result in harm to the patient, physician or hospital. It especially includes such orders as p.r.n., 'as necessary,' etc. The following classifications are ordinarily thought of as dangerous drugs: narcotics, sedatives, anticoagulants, and antibiotics."

Copies of the December 1957 issue of the Joint Commission on Accreditation of Hospitals *Bulletin* which lists the standards for the pharmacy department may be obtained by writing to the Joint Commission, 660 N. Rush St., Chicago 11, Illinois. The cost is 15 cents per copy and payment must accompany each request.

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

. . . . . .

edited by CLIFTON J. LATIOLAIS *and* LEO F. GODLEY

RUBBER CLOSURES, PROPERTIES

Rubber Diaphragms, A Preliminary Investigation into Some Properties of Six Different Rubber Samples, Weiffenbach, N. and Sorgdrager, P., Pharm. Weekblad 92:909 (Dec. 14) 1957.

The samples of rubber diaphragms (37 mm. diameter, 4 mm. thick) were investigated as follows:

Two discs (each one cut in four pieces) were autoclaved at 115° C with 100 ml. of distilled water for 45 minutes. The water was tested for pH (6.3-7.9), smell (faint), taste (slightly bitter to tasteless), appearance (clear and colorless to cloudy and brown), reducing substances (in 20 ml. equal to 2.17-26-84 ml of 0.01 N $KMnO_4$ and evaporation residue (in 20 ml; 1.5-3.5 mg.).

The same observations were repeated after the discs had been boiled for 15 minutes in a 5% sodium carbonate solution: pH 6.6-8.5, smell and taste and appearance unaltered, reducing substances in 20 ml equal to 2.17-26.35 ml 0.01 N $KMnO_4$ and evaporation residue in 20 ml 1.0-2.9 mg.

Next, the authors investigated the phenol absorption of the discs by autoclaving them in a 0.5% phenol solution at 115° C for 45 minutes. The phenol concentration after autoclaving was found to be 0.29-0.41%

In order to investigate the influence of certain drugs on the results, the observations were repeated with 100 ml of citrate mixture (citric acid 31.7 Gm. sodium citrate 156 Gm. - dextrose 50% 333 ml, and water q.s. ad 5000 ml). After autoclaving, all but one solution were clear and colorless; the reducing substances in 20 ml were equal to 13.16-18.08 ml and 0.1 N KMnO4, the evaporation residues of 20 ml weighed from 1.069-1.151 gram. The striking difference in appearance was not only caused by the pH of the Citrate mixture, as was proved by autoclaving the discs in an acetate buffer of pH 5.06. The pH after autoclaving ranged from 4.99 to 5.27, the appearance of the fluids being from clear and colorless to cloudy and brown.

J. WOUTER HUISMAN

CELLULOSE DISPERSIONS, FACTORS AFFECTING VISCOSITY

Water-Soluble Cellulose Derivatives, Factors Affecting the Viscosity of Aqueous Dispersions, Part I., Davies, R. T. M. and Rowson, J. M., J. Pharm. Pharmacol. 9:672 (Oct.) 1957.

This is a study of the effects of temperature and of the presence of acid and alkali on the viscosity of aqueous dispersions of methylcellulose, methylethylcellulose and sodium carboxymethylcellulose. Three viscosity grades, low, medium and high, of methylcellulose and sodium carboxymethylcellulose were studied while only one grade of methylethylcellulose was studied.

Dispersions of each cellulose derivative were heated to various temperatures ranging from 50° C to 115° C and the viscosity was measured after periods of heating ranging from 15 minutes to 4 hours. Both the methylcellulose and methylethylcellulose formed gels after reaching a temperature of 50°C but these gels would reverse to the original dispersion form upon cooling. The only samples of these two derivatives that showed any marked change in viscosity were the ones that were heated to 115° C for over an hour. Therefore, these derivatives of cellulose would be stable to heat for periods appropriate to a sterilization process. On the other hand, the sodium carboxymethylcellulose showed marked viscosity decrease upon very little heating for short periods of time.

Various samples of each derivative were made acidic and alkaline in a range of pH 1 to pH 12. The methylcellulose dispersions were stable except when the pH fell below 3. The methylethylcellulose samples were even more stable at wider range of pH while the sodium carboxymethylcellulose dispersions showed marked viscosity decrease when the pH fell below 5 or rose above 10.

RICHARD E. MARTIN

CELLULOSE DISPERSIONS, FACTORS AFFECTING VISCOSITY

Water-Soluble Cellulose Derivatives, Factors Affecting the Viscosity of Aqueous Dispersions. Part II, Davies, R. E. M. and Rowson, J. M., J. Pharm. Pharmacol. 10:30 (Jan.) 1958.

Methylcellulose and methylethylcellulose dispersions were unaffected by salt concentrations below 6%; however, when the salt concentration increased above this, the viscosity of these dispersions increased. Addition of salt to the sodium carboxymethylcellulose produced a decrease in viscosity. Alcohol, propylene glycol and glycerol increased the viscosities of all dispersions.

The surface-active agent, sodium lauryl sulfate, was added to all dispersions. It caused (1) a decrease in viscosity of the sodium carboxymethylcellulose dispersions; and (2) an initial increase in viscosity of the methylcellulose and methylethylcellulose dispersions followed by a decrease in viscosity upon larger concentrations of the agent being added.

Each type dispersion was also inoculated with a suspension of micro-organisms and each cellulose derivative was degraded to some extent. The sodium carboxymethylcellulose showed a much larger viscosity decrease than the other two derivatives.

Dispersions of all derivatives were stored for a year and the viscosities were then compared with the original viscosity. Methylcellulose of the low viscosity grade remained constant while the medium viscosity grade increased slightly and the high viscosity grade decreased. The methylethylcellulose dispersions all decreased in viscosity upon storage, The pH of all dispersions remained unchanged after being stored a year. Direct sunlight caused the sodium carboxymethylcellulose dispersion to darken upon storage.

RICHARD E. MARTIN

EMULSIONS

Pharmaceutical Emulsions, Chen, J. L., Cyr, G. M. and Langlykke, O. F., Drug and Cos. Ind. 81:596 (Nov.) 1957.

This is a review article on the general aspects of formulating and preparing pharmaceutical emulsions.

Dermatology has been more demanding of emulsions in the form of ointments, creams and lotions, than other branches of medicine. Cosmetics have used and continue to use a large variety of emulsion-type preparations. Emulsions used in dermatology must not only have good cosmetic appeal but they must be formulated with an eye to protecting the active medicinal. They should be water-washable and none of the incorporants should be sensitizers or primary irritants.

Pharmaceutical emulsions are made up of a dispersed phase, a dispersing agent, emulsifier, stabilizer and preservative. The proper vehicle is determined after a careful study of the active medicinal that is to be incorporated in the emulsion. Route of administration of the finished product also plays an important role. A high concentration of strong electrolytes is not conducive to stable emulsion formation.

Anionic, cationic and non-ionic surfactants as well as gums and hydrophilic clays have found suitable application in pharmaceutical emulsion preparation. Because non-ionic emulsifiers and stabilizers have a greater range of compatibility with active ingredients, they are to be favored in the manufacture of the pharmaceutical emulsion. Toxicity and sensitivity are less frequently encountered with the non-ionics. These latter emulsifiers are also less sensitive to electrolytes, have little effect on pH and produce an end product which is less likely to freeze. Pharmaceutical emulsifiers should be pure, non-toxic, non-irritating, non-sensitizing, odorless, tasteless, colorless and nearly neutral in pH.

Humectants are use to prevent drying during manufacture and storage. They also act as solubilizing agents

for other incorporants of hydrocolloids. The freezing point of the final product is lowered through the use of humectants.

Esters of parahydroxybenzoic acid are the most commonly used preservatives to prevent bacterial and mold growth in emulsions. Preservatives must be subjected to rigid tests when incorporated in the finished product to ascertain their antifungal and antibacterial effectiveness

Other agents which may be used in pharmaceutical emulsion systems are: antioxidants, foaming agents, antifoaming agents, buffers, chelating agents, complexing agents and solubilizers, as well as whitening agents and dyes.

The selected vehicle must be compatible with all of the emulsion ingredients and should be non-reactive with the primary medicinal agent. For example, tweens are known to reduce the effectiveness of preservatives, and phenolic compounds destroy the suspending power of several carbowax esters.

Accelerated aging test methods help to determine the type and rate of degradation of the active agent, optimum conditions for stability, best order of compounding, and proper selection of prepackaging materials. Because of the presence of so many ingredients in an emulsion system, aside from the active ingredient, assay procedures may at times present difficulties.

Pilot studies must relate in all respects to production since volume of operation has a bearing upon performance in emulsification. Production of uniform batches is dependent upon close adherence to the manufacturing formula as well as the finer details of procedure.

Glass is still the most widely used container for pharmaceutical emulsions. Creams seem to do better in tubes than in jars because of the greater protection against moisture loss. Polyethylene containers are gaining in popularity for creams and lotions; however, container collapse, due to the presence of certain ingredients, is not uncommon. Loss of volatile principles is also a consideration. Products sensitive to oxidation should not be stored in polyethylene containers because they tend to decompose rapidly.

Ultrasonic methods of emulsification seem to be in future grasp; however, large scale equipment adaptation is a problem. The application of sound energy may permit emulsification without the use of an emulsifying agent.

ED SUPERSTINE

OINTMENT BASES, INFLUENCE OF SURFACTANTS ON DRUG RELEASE FROM

A Comparative Study of Surfactant Influence on the Release of Radio-labeled Ions from an Emulsified Ointment Base, Stark, J. F., Dissertation Abstract 17:1356 (June) 1957.

An *in vitro* method, closely simulating actual conditions under which ointments are used, was developed to study the release of drugs from ointments using radioisotope labeled compounds.

Twenty-four surface active agents, anionic, cationic and nonionic, in three concentrations were used to formulate the ointment bases, which were modifications of USP XV hydrophilic ointment. Because of its ease and extreme sensitivity for detection, sodium iodide (I^{131}) and labeled mercuric nitrate (HG^{203}) were the analytical tools and represented the medicinal fraction of the ointment.

The data demonstrated that the release of the iodide and mercuric ions from the hydrophilic bases were retarded as the concentration of both the ionic and nonionic surfactants increased. It was assumed that the increased amount of surfactant tended to fortify the hydrophilic nature of the base, thus interfering and decreasing the ability of the emulsion base to release the water-soluble labeled drug. However, the nonionic group exhibited a more favorable diffusion and release of the labeled ions over the ionic surfactants.

NORMAN HO

OXIDATION OF BENZALDEHYDE IN DISPERSIONS

The Oxidation of Solubilized and Emulsified Oils. I. Oxidation of Benzaldehyde in Potassium Laurate and Cetomacrogol Dispersions, Carless, J. E. and Nixon, J. R., J. Pharm. Pharmacol. 9:963 (Dec.) 1957.

The oxidation of vitamins and volatile oils has been the subject of several research studies in the important application of the solubilization of water-insoluble organic substances with surface-active agents. The present study deals with the solubility and oxidation of benzaldehyde in the presence of two surface-active agents, potassium laurate and Cetomacrogol B.P.C. The water-soluble and oil-soluble catalysts, copper sulfate and copper laurate respectively, were selected to study the oxidation effect on benzaldehyde at the various phases of the solubilization process.

The solubility of benzaldehyde in solutions of the surface-active agents was measured at 20°C; the oxidation rates were determined manometrically at 25°C.

Increasing the amount of surface-active agents to benzaldehyde brought about the progressive change from a suspension, through an emulsion and on to a solubilized state. The rate of oxidation fell as the solubilized state was approached. The increase of catalytic copper concentration proportionately increased the rate of oxidation in the solubilized and emulsified states, the latter being more susceptible.

The loci of the oxidative reaction in the emulsion and solution state, that is, in the benzaldehyde phase, the benzaldehyde-water interface, and the water phase, were discussed. The experimental evidence suggested that most of the oxidation occurred in the benzaldehyde phase of the emulsion state. The possible reaction mechanisms of benzaldehyde, the copper catalysts, and the surface-active agents were also discussed.

NORMAN HO

MEDICINAL PLANTS

Chemical Races in Medicinal Plants, Evans, W. C., Pharm. J. 179:505 (Dec. 28) 1957.

Recent investigation has detected medicinal plant species which, while being phenotropically similar, yield a somewhat different chemical composition upon analysis. These different chemical races within a particular plant species are directly dependent upon the genetic combination of the plant and exist as a result of natural or artificial cross breeding of the species. Variances in the chemical composition have been reported in plant source species of many cyanogenic glycosides, alkaloids, anthraquinone mixtures, steroids, and volatile oils and cannot be explained on the basis of plant age, climate, or soil alone. Research has shown that these chemical races may be improved upon genetically to yield a drug of higher therapeutic value either by precise adjustment of the chemical constituents or by increasing the overall yield.

ROBERT MAHONEY

OINTMENT BASES, DIFFUSION OF MEDICINALS FROM SILICONE

A Comparison of In Vivo and In Vitro Tests for the Absorption, Penetration, and Diffusion of Some Medicinals from Silicone and Petrolatum Ointment Bases, Plein, J. B. and Plein, E. M., J. Am. Pharm. Assoc., Sci. Ed. 46:705 (Dec.) 1957.

In this study, five different medicinals were incorporated into several ointment bases and the diffusion, penetration and absorption of each medicinal from the ointment base were measured. The ointment bases used were petrolatum ointment and silicone ointment to represent the epidermic type, petrolatum absorption base and silicone absorption base to represent the endodermic type, and petrolatum emulsion base and silicone emulsion base to represent the diadermic type.

Medicinals incorporated into each base were sulfanilamide 10%, ammoniated mercury 5%, salicylic acid 5%, chlortetracycline hydrochloride 3%, and iodine 4%. Diffusion of the active ingredient from the base was measured by an agar plate test and by a chemical test. Penetration was measured by applying the ointment to the skin of a rat and waiting a period of time and then washing the excess ointment off. A biopsy of the inuncted skin was then taken and an analysis was done to determine the amount of medicinal that had penetrated the skin. Absorption was measured by doing similar analyses on the blood or the "storage organ" of the drug.

Sulfanilamide, chlortetracycline hydrochloride, and iodine, seemed to diffuse better from the emulsion type bases while the other two medicinals showed approximately the same amount of diffusion from all type bases. All of the drugs seemed to penetrate about the same from each of the bases. The chlortetracycline hydrochloride was absorbed much better from the emulsion type bases while the rest of the medicinals were absorbed equally well from all bases. It could not be shown that either silicone bases or petrolatum bases were more efficient.

RICHARD E. MARTIN

ESTIMATION OF SULFONAMIDES

Estimation of Sulfonamides, Gaind, K. N. and Punn, D. P., Indian J. Pharm. 19:279 (Dec.) 1957.

Most sulfonamides form acetylation derivatives in the body. This property was used as the basis for developing an acetylation method for estimating sulfonamide content in powder, tablet or injectable forms. This method consists of refluxing (on a sand bath) a known weight of substance with a known quantity of acetic anhydride in the presence of a few drops of pyridine.

The amount of unreacted acetic anhydride was determined by adding an excess of N sodium hydroxide and titrating the excess with 0.04 N sulfuric acid, using phenolphthalein as indicator.

The amount of sulfonamide was determined by multiplying the volume of sulfuric acid used in the titration with a factor for each sulfonamide. (This factor is based on the number of milligrams of sulfonamide equivalent to 1 ml. of 0.1 N sulfuric acid.) In all estimations a control experiment is necessary.

Estimation of sulfonamides by the acetylation method gave values between 95 percent and 100.2 percent of the theoretical.

CLIFTON J. LATIOLAIS

VOLUME TOLERANCES FOR MULTIPLE DOSE VIALS

A Study of Volume Tolerances for Multiple Dose Vials, Sperandio, G. J. and Belcastro, P. F., Bull. Parenteral Drug Assoc. 11:24 (Sept.-Oct.) 1957.

A study was made to determine how many doses may be withdrawn under normal conditions from 10 ml. and 30 ml. size vials containing mobile liquids. A number of 10 ml. and 30 ml. size vials were filled with exactly 10.5 ml. and 30.8 ml. of distilled water. These volumes conform to the U.S.P. allowance for excess of mobile liquid for vials of these sizes. It is pointed out that the U.S.P. makes no distinction between volume tolerances for single dose and multiple dose containers.

Nurses from different hospitals in four states participated in the study by attempting to withdraw the expected number of doses from these multiple dose vials.

Results indicate that there is a direct relationship between the number of withdrawals from a definite volume and the loss of liquid from the withdrawal process. The smaller the unit dose the more excess liquid is required to permit withdrawal of the expected number of doses. The authors are of the opinion that, under present U.S.P. requirements, overages for liquid in single dose vials may be found to be in excess of the amount needed, and overages for liquids in multiple dose vials may be insufficient in many cases.

The authors suggest that separate specifications be considered by the U.S.P. for tolerances allowed for liquids in single dose ampuls and in multiple dose vials and that consideration be given the manipulative errors of technique inherent to the withdrawal of fluids from multiple dose vials.

CLIFTON J. LATIOLAIS

CHELATION

Chelation and Its Application in Drug Chemistry, Albert, A., Australasian J. Pharm., 38:1158 (Oct.) 1957.

This review article is a discussion of the application of chelation in enzyme systems in cells, chemotherapy, poison-antidote therapy, and analytical methods. Chelation is a reaction between a complex-forming compound, chelating agent, and a metallic ion to form an organic metallic complex. The stability constant (obtained from mass action equations) of the chelating agent is an index of avidity for metallic ions, the greater the avidity the higher the constant.

That heavy metals (Cu, Fe, Mn, Ca, Mg, etc.), found in traces in cells, are necessary components of biologically active compounds and biochemical reactions have been established. Amino acids, peptides, nucleic acids, and some enzymes are metal-binders. In chemotherapy, experimental evidences seem to indicate that 8-hydroxyquinoline, isoniazid, and the tetracyclines owe their bactericidal activity to their highly chelating properties with the trace metals in bacteria cells.

Clinically, dimercaprol and the salts of ethylenediaminetetracetic acid are used as chelating antidotes for heavy metal poisonings. Salicylic acid is an effective antidote for beryllium poisoning; 2-mercaptoethylamine is successful in preventing radiation injury. As a chemical reagent, chelating agents are used for the identification and also the analysis of heavy metal cations.

NORMAN HO

EMULSION STABILITY

Phase Relations and Stability in Emulsions, Sumner, C. G., J. Appl. Chem. 7:504 (Sept.) 1957.

The continuous phase of an emulsion is the liquid in which the emulsifying agent is preferentially soluble or by which it is preferentially wetted. The barrier to the coalescence of the dispersed droplets, on contact, is an interfacially adsorbed film of emulsifying agent. It is still unknown why the same interfacial film hinders the coalescence of droplets of one liquid but not of the other.

Some workers have postulated that the coalescence of two droplets requires the localized displacement of stabilizer molecules at the interface which occurs if part of the film passes from the interface into the discontinuous phase. Stability will therefore be low if segments of the film are readily wetted by the liquid composing the droplets and vice versa.

The purpose of this paper was to suggest that irrespective of film displacement, the permeability of the interfacial film to the two liquids which constitute the main phases of the emulsion will determine which liquid can form persistent droplets within the other. The molecules of the permeable liquid diffuse through the interfacial film and coalesce. This permeability is further influenced by the closeness of packing of the emulsifier molecules in the interfacial film. In other words, droplets coming into close contact for a sufficient time can coalesce if the interfacial film does not completely inhibit diffusion of the dispersed phase.

This suggested mechanism is independent of the particular volume of the interfacial film, i.e., whether it is ionic or nonionic, unimolecular or miltimolecular in thickness, viscous or rigid, soluble or insoluble.

THEODORE J. BENYA

STERILIZING OVENS, TEMPERATURE VARIATIONS IN

Temperature Variation in Ovens Used for Sterilizing Pharmaceutical Products, Grainger, H. S. and Smith, M. D., Public Pharmacist, 15:39 (Jan.) 1958.

The performance of four types of electric ovens for dry heat sterilization was evaluated by means of thermocouples placed in various parts of the ovens and within the containers used. The electric ovens included: (1) a cylindrical one with the heating element in the back wall; (2) a rectangular oven with the heating element in the base; (3) a rectangular one with heating elements in the base and two sides; and (4) a rectangular one with the heating element in the base and a built-in fan in the back wall.

From the data, illustrated graphically, it was found that there existed a time-lag, which remains constant, for each type of pharmaceutical load in any oven to heat up, this being a factor of heat transfer. A thermometer was regarded as an unreliable guide to temperatures within an oven, for there were different readings obtained from thermometers and thermocouples. Uneven distribution of heat was noted in ovens without fans and with bottom heating with variations as much as 50°C. The necessity of a fan was realized to provide an even distribution of heat and a more rapid transfer of heat to containers. To indicate the importance of air spacing between containers, the results showed a long heating lag and a greater temperature difference when the circulation of air was impeded.

NORMAN HO

PURIFICATION OF RABIES VACCINE

Studies on the Purification of Rabies Vaccine Derived from Rabbit Brain, Gauthier, R. J., Dissertation Abstract 17:1187 (June) 1957.

Allergic encephalitis or other severe central nervous system reactions in individuals vaccinated with rabies vaccine derived from rabbit brain is believed to be an allergic reaction to the brain tissue in the vaccine. An investigation was undertaken to develop a method for the purification of the vaccine without an appreciable decrease of antigenicity of the vaccine.

The procedures, employing zinc precipitation and dissociation of the zinc complex with pH changes, failed to purify the vaccine without loss of antigenicity. It was found that rabies vaccine is very insoluble in aqueous or saline solutions due to the nature of the antigen itself or to the strong antigen—brain protein complex. Sonic oscillation increased the antigenicity of

the vaccine but no comparable increase in the antigen solubility was found. Repeated freezing and thawing completely destroyed the antigenic component and extractions with ether or a mixture of ether and alcohol at low temperatures resulted in a great loss of antigenicity.

It was concluded that the intimate association of the antigen with the rabbit brain substance resisted most physical and chemical methods of separation with denaturation of the antigen.

NORMAN HO

VITAMIN B_{12} STABILITY

The Stability of Vitamin B_{12}—Protection by Iron Salts Against Destruction by Aneurine and Nicotinamide, Mukherjee, S. L. and Sen, S. P., J. Pharm. Pharmacol. 9:759 (Nov.) 1957.

Solutions of vitamin B_{12} have been found to be stable, at an optimum pH range between 4 and 4.5 under normal storage conditions, for up to 18 months. However, in mixtures of vitamins containing aneurine and nicotinamide, there is marked deterioration of the B_{12} potency.

Studies have been made using iron as a stabilizer. Iron salts in general exert a protective action against the destructive action of aneurine and nicotinamide.

In an elevated temperature test the concentration of aneurine was lowered and when 15 ug./ml. of vitamin B_{12} was mixed with 2-15 mg./ml. of aneurine and 20-100 mg./ml. of nicotinamide, 95% of the B_{12} potency was destroyed.

In the tests eight iron salts were used in concentrations of 0.5 mg./ml.; these salts were iron and ammonium citrate, ferrous gluconate, ferric alum, ferrous alum, ferric chloride, potassium-ferric and ferric-cyanides, and ferrous sulfate.

It is concluded that the total loss of aneurine is about the same with or without the presence of iron salts, whereas B_{12} potency deteriorates only in the presence of aneurine and nicotinamide.

Iron salts in association with aneurine and nicotinamide without preventing the decomposition of aneurine, protect vitamin B_{12} in a specific way.

RICHARD H. HARRISON

STERILIZATION, STEAM

Sterilization of Fluids by Means of Steam Under Pressure, Owen, T. B., Am. J. Pharm. 129:425 (Dec.) 1957.

The application of steam under pressure as an agent for sterilizing flasked fluids is described briefly.

The sterilizing temperature usually employed is 250°F or 121°C, which is the temperature of saturated steam under 15 psig [pounds per square inch at ground (sea) level]. The temperature of 250°F is maintained by means of a thermostatic trap. This trap allows air and condensate to escape to the waste line, thereby maintaining proper sterilizing conditions throughout the entire exposure period.

Proper sterilizing conditions are solely dependent on time and temperature. Pressure alone is not enough. It is possible to have correct pressure but not enough temperature.

All sterilizer solution loads should be processed utilizing slow exhaust. Most sterilizers are equipped with controls to enable either a slow or fast exhaust.

For a given container a certain amount of time is required to raise the entire contents to the desired temperature. The innermost or center portion of the contents is the last to reach this temperature.

Steam in the process completely covers the outer surface of the container and in the case of a sealed container, will not come in contact with the inner area. Heat must be transferred by different methods; it is done by conduction and convection.

The entire contents must be raised to the desired temperature by these processes. The amount of time it takes to do so depends on the size and type of container and to some extent on the fluid.

During the sterilization process, the pressure both in the chamber and inside the container becomes equalized. Thus, it is necessary to utilize a slow exhaust. Some containers are equipped with a vented closure to enable an equalized reduction in pressure.

Extreme caution should be taken to permit a slow, gradual cooling of hermetically sealed containers at the end of the sterilizing process.

RICHARD H. HARRISON

PARENTERALS, EFFECTS OF PLASTICS ON

The Effects of Plastics on Parenteral Products, Autian, J., Bull. Parenteral Drug Assoc. 11:25 (Nov.-Dec.) 1957.

The author discussed problems which may arise when synthetic thermoplastics, such as polyethylene, polystyrene and nylon, are utilized for parenteral products.

Permeability studies reveal that loss of vial contents or entrance of gases from the atmosphere may occur with polyethylene containers. Transmission of solvents through polyethylene depends upon the size, shape and polarity of these solvent molecules. The following list of solvents is arranged in order of increasing transmission rate: alcohol, acids, nitroderivatives, aldehydes, ketones, ether, hydrocarbons. The passage of gases through a polyethylene film shows no simple relationship between rate of diffusion and density of film. Oxidation of vial contents may occur with the entry of oxygen. Also, transmission of carbon dioxide may lower pH sufficiently to cause precipitation of salts of weak bases.

Certain drugs will react chemically with plastics. Nylon, with recurring polar oxygen atoms in its structure, may form hydrogen bonds with weak acids; thus, phenols are formed as a result of this reaction. Polystyrene is adversely affected by certain chlorinated hydrocarbons. Aqueous solutions of Metrazol exert a solvent action on many plastics. Chlorothymol loses its potency when packaged in plastics.

The electrostatic charge associated with many plastics produces difficulties in cleaning due to the adherence of lint particles.

Additives incorporated in plastics to improve their physical properties may present problems of toxicity. These substances may leak out, producing unfavorable reactions in patients.

JOHN LUCASSE

STERILIZATION, GAS

Gas Sterilization of Packaged Disposable Units, Glen, W. K., Bull. Parenteral Drug Assoc. 11:30 (Nov.-Dec.) 1957.

Gas sterilization utilizing ethylene oxide is becoming more widespread as the use of disposable intravenous sets and similar units increases. Thus, the efficient operation of a gas sterilizer takes on added importance. Five factors related to this operation are discussed: (1) Permeability of packaging material; (2) Concentration of ethylene oxide (C_2H_4O); (3) Pressure differential; (4) Humidity; and (5) Temperature.

Tests on paper and plastic films used in packaging disposable units show that their permeability to ethylene oxide differs greatly. Few types of plastic films are impermeable. Data regarding permeability of any specific film can be obtained from its manufacturer. Concentration of ethylene oxide used in effective gas sterilization has ranged from 10% to 100%. A mixture which can be safely used under pressure is 20% ethylene oxide and 80% carbon dioxide. In gas sterilization, regulation of pressure differential is essential. An initial vacuum is used to remove air from the packages. This is followed by pressure to introduce the sterilizing gas and a secondary vacuum to remove the gas. Lack of sufficient humidity will adversely affect the time needed for sterilization. The optimum relative humidity varies from 20% to 40% depending upon the nature of the sterilizer load. Temperature must be controlled in gas sterilization from the standpoint of kill of organisms and of damage to packaging films. For every 30°F temperature rise the killing time is reduced by one-half. However, maximum temperature limits for each type of packaging film must be considered before establishing an optimum temperature for any sterilizer load.

JOHN LUCASSE

FILTERED AIR FOR STERILE ROOMS

Filtered Air Supplies for Sterile Rooms, Carter, D. V., Public Pharm. (Great Britain) 14:230 (Oct.) 1957.

To supply an aseptic room with treated air, an exchange rate of at least 6 to 12 per hour is desirable. Since such an installation may prove too costly, a filter system supplying near sterile air is installed in most instances. The expense of installation may be further reduced by giving attention to that area in the immediate vicinity of the actual aseptic manipulations, by flushing this area during operations with a flow of sterile air equal to at least one exchange per minute.

Different methods of supplying sterile air were considered, namely mechanical filtration, chemical treatment (scrubbing or spray methods), radiation, electrostatic precipation and heat.

From the standpoint of overall cost and high efficiency mechanical filtration of air contaminants appears to be the most practical method. Efficiencies approaching 100% may be obtained when the operating pressure approaches 1 to 5 pounds per square inch and with the use of a properly designed filter consisting of fine grade steel or glass wool packed to a proper depth and density. In the case of glass wool, the filter bed is packed to a depth of 6 inches, to a density of 16 pounds per cubic foot.

High efficiency can be maintained only through regular examination and exchange of filters. No fixed period or hard rule can be given since conditions of usage vary widely. However, in light industrial areas a glass fiber filter should be exchanged every 4 to 8 weeks where it is in use 8 hours a day.

ARTHUR GIBSON

PREPARATION OF PEPSIN-CONTAINING LIQUID MIXTURES

Experiences with the Preparation of Pepsin Mixtures, Aslonov, G. K., Aptechnoe Delo (U.S.S.R.) 6, 4:18 (July-Aug.) 1957.

When preparing pepsin and hydrochloric acid-containing liquid mixtures, it is necessary to dissolve the pepsin only after dilution of the hydrochloric acid with all water prescribed. By solution of pepsin in hydrochloric acid before dilution of the latter, a partial or total decomposition of pepsin is caused.

The author has found that the 0.25% concentration of hydrochloric acid in a mixture is the best for the digestive potency of pepsin. A stronger concentration of hydrochloric acid effects a loss of digestive activity of pepsin.

It is warned against filtering the pepsin-containing liquid mixtures through cotton-wool tampons or paper filters because of adsorption of pepsin on both latter objects. When filtration is desirable, a glass filter should be used.

HUBERT ZACEK

ULTRASOUND FOR PREPARING SUSPENSIONS

A Study of Dispersion With Ultrasound I, Misek, B., and Skauen, D. M., J. Am. Pharm. Assoc., Sci. Ed., 47:32 (Jan.) 1958.

Experiments on the use of ultrasonic energy for mechanically dispersing crystalline solids in liquid media is reported. Using a quartz crystal piezoelectric transducer, the effects of intensity and duration of insonation on various concentrations of progesterone crystals of known particle size in aqueous Superinone solutions were studied. Results showed that progesterone is stable to ultrasonic treatment; that dispersion is much more efficient if a wetting agent is added to the system; that concentration of the dispersed material has no effect on the final particle size; that the final particle size was directly proportional to the initial particle size after a standard period of insonation; that there was an optimum period of insonation which produced maximum dispersion and that the degree of dispersion was directly related to the intensity of insonation.

WARREN E. MCCONNELL

ULTRASOUND FOR PREPARING SUSPENSIONS

A Study of Dispersion With Ultrasound II, Misek, B., and Skauen, D. M., J. Am. Pharm. Assoc., Sci. Ed., 47:36 (Jan.) 1958.

Continuing with their study of the use of ultrasonic energy for dispersion of solids in liquid media, these investigators show that the extent of dispersion of progesterone in aqueous Superinone solution was hindered by increasing the viscosity of the suspending medium but was increased if the treatment vessel was pressurized to a certain extent. They further report that the temperature of the liquid being treated had little effect on dispersion, nor did the frequency of the ultrasonic energy which was used for the treatment.

WARREN E. MCCONNELL

ANTIPERSPIRANTS

The Study of the Effect of Certain Chemicals on Perspiration Flow, Collins, G. F., and Christian, J. E., J. Am. Pharm. Assoc., Sci. Ed., 47:25 (Jan.) 1958.

Using a procedure which they had developed for the evaluation of antiperspirant preparations, these authors report on the antiperspirant effectiveness of several newly synthesized compounds. Statistically evaluated results are reported which show that all of these compounds—lanthanum sulfamate, lanthanum methionate, cerous methionate, aluminum methionate and cerous sulfamate—are more effective antiperspirants than 25% aluminum sulfate solution or any of a number of commercial antiperspirant creams tested. The authors point out that the antiperspirant effectiveness of salts of trivalent ions is directly related to the position of the ion in the Holfmeister or lyotropic series.

WARREN E. MCCONNELL

OINTMENT BASES

Certain Metallic Soap-Petrolatum Ointment Bases, Singiser, R. E., and Beal, H. M., J. Am. Pharm. Assoc., Sci. Ed., 47:6 (Jan.) 1958.

This study dealt with attempts to modify the rheologic behavior of petrolatum ointment bases in order to broaden the temperature range over which they would be pharmaceutically stable. Three base constituents—liquid petrolatum, petrolatum, and petrolatum plus wool fat—were individually modified by combining with each of eight different metal soaps. The resulting products were stored at temperatures from 8° to 45°C. Ointment consistencies were periodically measured by means of a penetrometer. Results showed that Aero aluminum stearate G-100 yielded ointments having optimum thermal stability when combined with any of the three base constituents. Compatibility of these bases with most medicants tested was reported to be better than with petrolatum alone.

WARREN E. MCCONNELL

VITAMIN B_{12} STABILITY

Cyanocobalamin (Vitamin B_{12}) II. Further Studies of the Effect of Ascorbic Acid Degradation Products on Cyanocobalamin, Bartilucci, A. J. DiGirolamo, R., and Eisen, H., J. Am. Pharm. Assoc., Sci. Ed., 47:42 (Jan.) 1958.

Experiments are described which indicate that cyanocobalamin is not stable in the presence of dehydroascorbic acid, a decomposition product of ascorbic acid. As the concentration of dehydroascorbic acid increases, the stability of cyanocobalamin decreases.

WARREN E. MCCONNELL

IMPROVING COMPATIBILITY OF METHYLCELLULOSE

The Effect of Certain Additives on the Gel Point of Methylcellulose, Levy, G., and Schwarz, T. W., J. Am. Pharm. Assoc., Sci. Ed., 47:44 (Jan.) 1958.

The temperature to which a solution of methylcellulose must be raised in order to cause the dissolved methylcellulose to precipitate and form a viscous mass is called its "*gel point.*" Many electrolytes and some non-electrolytes will bring about a decrease in the gel point of methylcellulose solutions while some other materials will cause the gel point to raise.

The purpose of this study was to investigate further the effects of certain pharmaceutically acceptable additives which could be used to counteract the gel point depressing effects of other materials. Results showed that ethanol, propylene glycol, and polyethylene glycol each had the desired effect. An explanation is offered for the apparently anomalous effects of different polyols on the gel point of methylcellulose solutions.

WARREN E. MCCONNELL

EFFICIENCY OF BOTTLE CAPS AS MOISTURE BARRIERS

A Study of Moisture Vapor Transmission Through Closures, Blaug, S. M., Hickman, E., and Lach, J. L., J. Am. Pharm. Assoc., Sci. Ed., 47:54 (Jan.) 1958.

A problem occurring in the packaging of pharmaceuticals which must be protected from moisture is the transmission of moisture through the bottle caps and liners. The stability of hygroscopic materials or materials which decompose in the presence of moisture, such as ascorbic acid, may be significantly impaired by the amount of moisture gaining access to a bottle through its cap liner. Experiments were conducted to determine the effect of moisture upon caps and cap liners of various compositions. Results indicated that metal closures are generally more satisfactory than plastic closures as moisture barriers. The lower efficiency of plastic closures is attributed to the "backoff" tendency or

slow unscrewing of the closures due to expansion of the closures in a humid atmosphere. Of sixteen liner materials investigated, polyethylene, aluminum foil, plastic-wax saturated pulpboard, and red rubber liners were found to be the most effective moisture vapor barriers, particularly when used in metal closures.

WARREN E. MCCONNELL

NEW ORGANIZATIONAL CHART

Mapping the Executive Setup, Business Week, April 6, 1957, page 187.

The latest thing in diagrammatic gadgets is a new linear chart originally devised and developed by a Dutch consultant. In a corporate, divisional or departmental hierarchy, it is designed to show at a glance (1) executives' specific functions and (2) their responsibilities to other executives. It has already gained popularity with 30 U. S. companies including Corning Glass Works, Gamble Brothers, and Sears, Roebuck subsidiaries with many more considering its adoption.

Proponents claim it's a big improvement over older methods such as the conventional pyramidal chart and manual. The pyramidal chart adequately illustrates the chain of command, but doesn't report who makes specific decisions and therefore must be supplemented by recourse to a voluminous organizational manual.

As its principal virtues, supporters boast that in one minute an executive can be educated as to how many others he must consult—or deter to—in a variety of areas, that it is conveniently flexible in keeping up with changes in organization, that it is a helpful device in considering the effect of change on the organization and that it clearly defines a man's job, thereby eliminating jurisdictional disputes.

As a possible disadvantage, it was pointed out that it is only a tool. As such it has drawbacks common to all such mechanical aids in management—just because the chart says something doesn't make it true. In many organizations it is extremely difficult or impossible to determine exactly who does what, and although this chart helps to pin down specific functions, it cannot show that which the chart maker himself doesn't know.

It can be concluded that the linear chart promises to be a handy guide to formal job functions and interrelationships.

LEWIS C. MINER

SELECTION OF FILTERS FOR PARENTERALS

The Selection of Filters for the Filtration of Parenteral Solutions, Avis, K. E., Am. J. Pharm. 129:410 (Nov.) 1957.

Filters are selected to achieve (1) clarification or (2) bacterial-free filtrates plus clarification. Filters function by one or a combination of (1) sieving or screening, (2) entrapment in tortuous passageways, or (3) electrostatic attraction. For clarification the pore diameter of the filtrate should be less than 10 microns. To obtain bacterial filtrates the pore diameter should be about 2 microns or less.

Rate of filtration is affected by (1) the greater number of pores per unit area of filter surface, the more rapid the rate, (2) the greater the viscosity of the solution, the slower the rate, and (3) the difference in pressure on the two sides of the filter medium (vacuum or pressure) increases the rate. Loss of solvent occurs due to evaporation when solution is filtered under vacuum, thus producing a more concentrated solution. Optimum circumstances for fast filtration must be sacrificed when bacterial-free filtrates are desired.

Because of chemical or electro-chemical natures of filter media, the filter may also (1) alter pH of filtrate, or (2) adsorb and remove active medicinal from solution, especially dyes, alkaloids or glycosides.

Filters of different characteristics are available in a range of pore sizes for bacterial filtration and/or clarification. Sintered glass filters do not affect pH of filtrate and do not adsorb drugs. Unglazed porcelain filters are relatively strong and may be cleaned by ignition. Diatomaceous earth filters are more fragile, more adsorptive, and less chemically inert. Asbestos pad filters, while disposable, also adsorb medicinals and impart alkalinity. Sintered metal filters are effective, but not useful for solutions affected by metallic ions. Cellulose membrane filters are chemically inert and effective but useful only for very small volumes because the pores are small and easily plugged.

DON E. FRANCKE

LINEAR ORGANIZATIONAL CHART

	BOARD	PRES.	VP FINANCE	VP MARKETING	VP ADVERTISING	LEGAL COUNSEL	VP MGFERNG	OTHERS ETC.
Establish Overall Objectives	B	A	E	E		E	E	
Approve Overall Plans	B	A	E	E		G	E	
Direct Overall Operations	B	A	G	G		G	G	
Approve Expansion Plans	B	A	E	E		F	E	
Coordinate Line and Staff	B	A	E	E		E	E	
Decide on Tax Matters		B	A			G		
Coordinate Budget	F	B	A	E			E	
Determine Financial Needs		B	A					
Determine Marketing Policies		B		A	G			
Overall Sales Forecast	F	B	F	A			F	
Coordinate Production Expans.		B	E	A			E	
Plan Advertising	F	D	E	B	A		G	
Administer Legal Matters		B	G			A		

A—Actual Job Responsibility
B—General Supervision
C—Direct Supervision
D—Decide on Specific Points
E—Must be Consulted
F—Must be Notified
G—May be called in

SIZE OF SOME AMERICAN PHARMACEUTICAL COMPANIES
AS REPORTED IN THE JULY 1957 SUPPLEMENT TO FORTUNE MAGAZINE

RANK	COMPANY	SALES (000,000)	ASSETS (000,000)	NET PROFIT (000)	INVESTED CAPITAL (000,00)	STOCKHOLDERS	EMPLOYEES	PROFIT AS SALES	PERCENT OF INV. CAPITAL
215	Lilly	182	196 (142)*	30,053 (82)*	153 (110)*	4,800 (110)*	8,438 (247)*	16.6 (13)*	19.17 (65)*
218	Pfizer	178	156 (179)	18,254 (121)	115 (147)	24,000 (106)	9,500 (215)	10.2 (68)	15.9 (137)
220	Sterling	178	146 (192)	16,919 (128)	85 (200)	36,000 (67)	12,771 (157)	9.5 (78)	20.0 (56)
227	Merck	172	168 (168)	20,224 (109)	138 (120)	25,000 (101)	10,150 (199)	11.7 (36)	14.7 (171)
233	Mead	168	145 (197)	13,385 (164)	94 (188)	6,109 (328)	7,230 (284)	8.0 (129)	14.2 (191)
250	Rexall Drug	156	91 (283)	4,474 (360)	49 (329)	15,865 (161)	9,500 (216)	2.9 (403)	9.2 (363)
277	Parke Davis	134	139 (208)	17,646 (125)	103 (169)	25,457 (99)	9,895 (212)	13.2 (28)	17.2 (103)
337	Smith, Kline and French	105	71 (337)	18,879 (117)	44 (348)	5,859 (338)	2,200 (470)	18.1 (12)	42.5 (3)

*Figure in parentheses indicates rank of firm in particular category

SIZE OF U. S. PHARMACEUTICAL CORPORATIONS

The 500 Largest U. S. Industrial Corporations, and the 50 Largest Banks, Merchandising, Transportation, Life Insurance, and Utility Companies, and the 100 Largest Foreign Industrial Corporations, Supplement to Fortune Magazine (July) 1957.

The 500 largest U. S. industrial corporations, an annual publication of *Fortune Magazine*, selects and ranks corporations on the basis of sales for each fiscal year ending January 2. Only firms deriving at least 50% total revenue from manufacturing and/or mining are listed. The directory gives for each firm listed: (1) Rank, (2) Headquarters, (3) Sales, (4) Total assets, (5) Profits after taxes, (6) Invested capital (net worth), (7) Number of stockholders, (8) Number of employees, (9) Profit as percent of sales, and (10) Profit as percent of invested capital.

The pharmaceutical manufacturers included in the listing were: Eli Lilly, Charles Pfizer, Sterling Drug, Merck Sharp & Dohme, Mead Johnson, Rexall Drug, Parke Davis, and Smith, Kline and French. Lilly, with sales of $181,530,000.00, was ranked number 215 and was the largest in the pharmaceutical group. Smith, Kline and French, the smallest, was ranked number 337 with sales of $104,609,000.00.

Following is a table giving the figures of the pharmaceutical firms listed.

Analysis of the table reveals some interesting facts concerning the pharmaceutical firms. All, excluding Smith, Kline and French, are ranked fairly close together, the range being from 215 to 277. Also, with the exception of Rexall, all rank higher as to net profit than to sales. The same holds true for the categories, invested capital, profit as percent of sales and profit as percent of invested capital. For example, even though Smith, Kline and French is 337th in total volume of sales, it ranks 12th in profit as percent of sales and 3rd in profit as percent of invested capital. From the column profit as percent of sales it can be seen that the profit realized from sale of drugs is high. Likewise the column profit as percent of invested capital indicates return on investment is relatively high in pharmaceutical manufacturing.

JOHN D. LUCASSE

SOLUBILIZATION OF VITAMINS A AND D

Studies on Pharmaceutical Preparations. VI. Solubilization of Vitamin A and D. (2). Solubilization with Hydrogenated Castor Oil Polyethylene Glycol Derivatives, Mima, H., Asahi, Y, and Kanzawa, T., J. Pharm. Soc. Japan, 77:1201 (Nov.) 1957.

Solubilization of vitamins A and D has been effected by the use of surface active agents such as Tween, Myrj, and Brij, but recently it has been found that the solubilization can be effected by the use of hydrogenated castor oil polyethylene glycol ether (HCO). In this case the best active agent differs with the kind of vitamin A and D. HCO of low polymerization degree was found to be suitable for vitamin A palmitate, while that of high polymerization degree was better for vitamin A alcohol and D. Some of HCO were found to have greater range of solubilization than Tween, Myrj, or Brij. HCO derived from hydrogenated castor oil was less toxic than that derived from non-hydrogenated castor oil. Especially, HCO of high polymerization degree was less toxic than Tween. Although hemolytic action of HCO was slightly stronger than Tween, Atlas G 1295 is low in toxicity and therefore suitable for injection. The irritation or pain caused by injection of HCO was not different from those caused by injection of Tween, but the taste of the former was better. From these results HCO was found to be a good solubilizing agent.

AUTHOR'S SUMMARY

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

ADMINISTRATION

—Policies

Jeffrey, Louis P.: The Pharmacy Should Control Drug Samples, *Modern Hosp.* 90:90 (Feb.) 1958.

DEPARTMENTS

Stephen, R. A.: St. Joseph's of London Sets up New Pharmacy, *Hosp. Pharm.* (Canada) 10:303 (Nov.-Dec.) 1957.

INTERNATIONAL

Reinstein, Jerome A.: International Pharmaceutical Students' Federation, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 19:88 (Feb.) 1958.

NARCOTICS

Oddis, J. A.: Narcotics and Disaster Plans (Service from Headquarters), *Hospitals* 32:20 (Feb. 1) 1958.

PHARMACY AND THERAPEUTICS COMMITTEE

LaNier, J. Conklin II: The Formulary Problem (Part I), *The Rocky Mountain Druggist* 68:32 (Aug.) 1957.

LaNier, J. Conklin II: The Formulary Problem (Part II), *The Rocky Mountain Druggist* 68:14 (Oct.) 1957.

LaNier, J. Conklin II: The Formulary Problem (Part III), *The Rocky Mountain Druggist* 68:30 (Nov.) 1957.

Ponka, Joseph L.: The Operations of a Pharmacy Formulary Committee, *Hosp. Management* 85:110 (Feb.) 1958.

PURCHASING

Sister Eugene Marie: Purchasing—Success Formula: Central Purchasing Plus Close Stock Control, *Hospitals* 32:60 (Feb. 16) 1958.

—Prepackaging

Graham, Reuben H.: Hospitals Control the Trend of Prepackaging, *Hosp. Management* 85:126 (Feb.) 1958.

PROFESSIONAL RELATIONS

Bellafiore, Ignatius J.: Therapeutic Consultant, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 19:90 (Feb.) 1958.

STANDARDS

Parker, Paul F.: (Division of Hospital Pharmacy) Accreditation Standards, *J. Am. Pharm. Assoc., Pract. Pharm. Ed.* 19:95 (Feb.) 1958.

Joint Commission on Accreditation of Hospitals: Standards of the Joint Commission on Hospitals (Reprinted from Bulletin 16 of the Joint Commission on Accreditation of Hospitals, December 1957), *Hosp. Management* 85:115 (Feb.) 1958.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *Journal* to February 1, 1958.

Notice

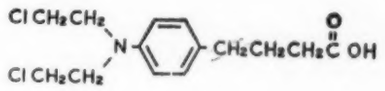
New and Nonofficial Remedies 1958 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1958 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to October 1957. The index listed below contains those drugs evaluated and published between October 1, 1957 and February 1, 1958.

INDEX TO DRUGS EVALUATED IN THIS ISSUE

INDEX TO EVALUATED DRUGS PUBLISHED IN THE JANUARY AND FEBRUARY 1958 ISSUES OF THE AMERICAN JOURNAL OF HOSPITAL PHARMACY.

Chlorambucil — Leukeran®

CHLORAMBUCIL is 4-{*p*-[Bis(2-chloroethyl)amino]phenyl}-butyric acid. The structural formula of chlorambucil may be represented as follows:



Actions and Uses

Chlorambucil, a nitrogen mustard derivative, has actions and uses similar to those of mechlorethamine hydrochloride (HN_2) and triethylene melamine. The drug is effective by the oral route and is more completely absorbed from the gastrointestinal tract than is triethylene melamine. After the administration of large doses to experimental animals, chlorambucil produces cytotoxic effects that are typical of the nitrogen mustards. In clinical employment, however, its pharmacological effects are restricted primarily to hematopoietic tissue. Although the drug is by no means completely selective in its action, it does depress lymphocytic proliferation and maturation to a much greater extent than that of the granulocytic elements. Side-effects, such as anorexia, nausea, and vomiting, which almost always complicate therapy with mechlorethamine and frequently appear with triethylene melamine also, occur only rarely with chlorambucil.

Chlorambucil is useful for the palliative treatment of chronic lymphocytic leukemia, lymphosarcoma, and Hodgkin's disease. Although there is little evidence that the drug appreciably increases survival time of patients with any of these diseases, it produces remissions of variable duration in a sizable proportion of patients. The drug is more effective if used in the generalized, but not terminal, stages of these diseases; radiation therapy is generally considered preferable for the initial treatment of early or localized lesions. However, chlorambucil is capable of inducing remissions in some patients who are refractory to radiation, and it may also be used effectively when the neoplastic involvement is too widespread to be amenable to radiation therapy.

As with all other chemotherapeutic agents, each course of therapy with chlorambucil is likely to be less effective than the preceding one. Remissions due to chlorambucil are characterized by relief of pain and pruritus, partial and

temporary regression of soft-tissue lesions and enlarged lymph nodes, reduction in hepatomegaly and splenomegaly, lessening of existing anemia, weight gain, and general feeling of well-being. In patients with chronic lymphocytic leukemia, marked hematological improvement may occur in conjunction with clinical remissions. Thus, the drug produces a rapid reduction in total leukocyte count, acting primarily on the lymphocytic elements. Although there is no evidence that chlorambucil exerts a greater antineoplastic effect than any other cytotoxic drug, the fact that it is absorbed in a more predictable manner, produces fewer side-effects, and may be less damaging to the bone marrow makes it somewhat easier to handle than either mechlorethamine hydrochloride or triethylene melamine. Hence, from the point of view of patient tolerance and ease of management, chlorambucil appears to compare favorably with other chemotherapeutic agents.

It is still too early to determine the possible usefulness of chlorambucil in mycosis fungoides or bronchogenic carcinoma. The drug apparently is of no value in chronic granulocytic leukemia or in any type of acute leukemia.

Apart from occasional instances of gastric distress, the clinical toxicity of chlorambucil is related entirely to bone marrow depression. Depending on dosage and duration of therapy, lymphopenia, neutropenia, and thrombocytopenia may appear in that order of occurrence. Unless dosage is reduced or the drug discontinued, irreversible damage to the bone marrow may result. Hence, it is imperative that the hematological status of the patient be carefully followed during treatment. Complete blood examinations, including erythrocyte count, hemoglobin level, and total and differential leukocyte counts, are mandatory at least once a week preferably more often. Thrombocyte estimations are also indicated at regular intervals or at the first sign of abnormal bleeding tendencies.

Although it is not necessary to discontinue therapy at the first evidence of a fall in the neutrophil count, it should be remembered that the fall may continue for 10 days after the last dose and that, as the total dose approaches 6.5 mg. per kilogram of body weight, there is real danger of causing irreversible bone marrow damage. Chlorambucil should not be given to patients with severe leukopenia, thrombocytopenia, or anemia due either to direct invasion of bone marrow by tumor cells or to previous therapy with depressant drugs or ionizing radiation.

Dosage

Chlorambucil is administered orally. For the initiation of therapy in patients with Hodgkin's disease, the usual dose is 0.2 mg. per kilogram of body weight daily for three to six weeks as required. Patients with lymphosarcoma or chronic lymphocytic leukemia usually require about 0.1 mg. per kilogram of body weight per day for a similar period of time. It should be emphasized that the foregoing dosages are only approximate averages and that dosage for each particular patient should be individualized according to clinical and hematological response. If a remission is obtained, many authorities favor discontinuation of all medication until relapse occurs. However, if maintenance therapy during remission is considered advisable, the dosage for this purpose should not exceed 0.1 mg. per kilogram of body weight each day and may well be as low as 0.03 mg. per kilogram of body weight daily.

Preparations: tablets 2 mg.
Applicable commercial name: Leukeran.
Burroughs Wellcome & Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of chlorambucil.
***J.A.M.A. 166*:50 (Jan. 4) 1958**

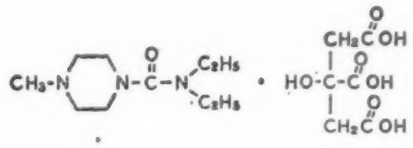
Preparations

Tablets Chlorambucil (Leukeran) 2 mg., sugar-coated.

Diethylcarbamazine Citrate U.S.P.

Hetrazan® Citrate

DIETHYLCARBAMAZINE CITRATE, U.S.P. is N,N,-diethyl-4-methyl-1-piperazine carboxamide dihydrogen citrate. 1-Diethylcarbamyl-4-methylpiperazine dihydrogen citrate. The structural formula of diethylcarbamazine citrate may be represented as follows:



Actions and Uses

Diethylcarbamazine citrate is a piperazine derivative with pronounced activity against the microfilarial larvae of certain filarial nematodes. It finds its widest use in the treatment of infestations due to Wuchereria bancrofti (Bancroftian filariasis) and, at the present time, is considered the most useful agent available for the chemotherapy of this disease. In both experimental animals and human patients, the drug causes a rapid disappearance of microfilariae. By suppressing or eliminating the microfilariae, diethylcarbamazine also interrupts vector (mosquito) transmission. The extent to which adult worms are killed by this drug is not known. However, if adequate therapy is given, microfilariae do not reappear in the blood in the majority of patients. The type of radical cure thus effected suggests a lethal action against the adult worms of W. bancrofti. Diethylcarbamazine apparently is equally as effective in the treatment of infestations due to W. malayi (Malayan filariasis). In view of its oral effectiveness, high order of therapeutic efficacy, and relative lack of serious toxic effects, diethylcarbamazine is considered preferable to the older anthelmintics containing antimony or arsenic for the treatment of filariasis.

Diethylcarbamazine citrate also kills the microfilariae of Onchocerca volvulus. It is therefore useful for the control of acute symptoms of onchocerciasis, particularly in cases with secondary cutaneous or subcutaneous ophthalmic lesions. Unlike its action in filariasis, the drug exerts no lethal or sterilizing effects against the adult worms of O. volvulus; hence, large numbers of microfilariae reappear after therapy is terminated. For this reason, diethylcarbamazine is not considered a curative agent for onchocerciasis. In occasional cases, it may be possible to effect a permanent cure by concomitant administration of the drug and surgical excision of the nodular lesions which contain the adult worms. (Although not without danger to the patient, suramin sodium is the only available agent which is effective for the radical cure of onchocerciasis. When administered intravenously, this drug causes the slow disintegration and death of the adult worms as well as the microfilariae, thus eliminating the infestation.)

Caution should be exercised in administering diethylcarbamazine to patients with onchocerciasis, since severe reactions after a single dose may appear, depending apparently upon the severity of the infestation. Facial edema, pruritus, itching of the eyes, and other signs suggestive of foreign protein reaction may occur. It is believed that these effects are as much due to the mass destruction and absorption of worm bodies as to an inherent toxicity of the drug. Therapy should be discontinued and antihistamine drugs administered at the first sign of such reactions; reinitiation of diethylcarbamazine therapy, if indicated, should be on a cautious basis and in reduced dosage. In severe infestations, especially ocular, maximal dosage should be attained gradually.

Loa loa parasitism (loiasis) is reported to be amenable to therapy with diethylcarbamazine citrate. The drug causes a disappearance of microfilariae and kills adult worms; adequate therapy will therefore result in cure in most cases.

The drug has also been employed for the treatment of creeping eruption (cutaneous larvæ migrans) due to Ancylostoma braziliense and, less commonly, A. caninum. Although a few reports have been favorable, there is insufficient evidence at hand to establish the ultimate therapeutic value of the drug in this self-limited nematode infestation. Some evidence suggests that the drug may relieve the pruritus associated with this infestation. Diethylcarbamazine is not effective against adult hookworms, whipworms, tapeworms, or pinworms. Its value in other filarial infestations caused by Acanthocheilonema perstans. A. streptocerca, and Mansonella ozzardi is not established.

Diethylcarbamazine citrate has been used in the treatment of infestations due to roundworms (Ascaris lumbricoides). The drug causes the expulsion of some ascarides by the second day of treatment, but a single course of therapy lasting four days rarely results in the removal of all worms. Since it offers no advantages over piperazine from the standpoint of toxicity and since it is definitely less effective, the employment of diethylcarbamazine for the treatment of ascariasis is justified only in situations in which piperazine is not available or in which sensitivity precludes the use of piperazine.

The toxicity of diethylcarbamazine citrate in experimental animals is low. When used clinically, however, the drug frequently produces side-effects. These are usually of short duration and, except for patients with onchocerciasis, are generally not of a serious nature. Fever, leukocytosis, and lymphadenitis commonly occur during a course of therapy for filariasis. Likewise, headache, lassitude and malaise, nausea and vomiting, and skin rashes are also encountered, in that order of frequency. Except for severe allergic phenomena in conjunction with skin rashes, it is usually not necessary to discontinue medication since most of the other side-effects are transient.

Dosage

Diethylcarbamazine citrate is administered orally, preferably after meals. For the treatment of filariasis, loa loa parasitism, and creeping eruption, the usual dose for adults is 2 mg. per kilogram of body weight three times daily. In acute cases, therapy should be continued for three or four weeks. For the treatment of acute symptoms of onchocerciasis, the suggested dose is 2 mg. per kilogram of body weight given once on the first day, twice on the second day, and three times daily for the next 30 days. In the treatment of ascariasis, the usual course of therapy consists of 13 mg. per kilogram of body weight once daily for four days.

Preparations: syrup 10 mg. in 1 cc.; tablets 50 mg.
Applicable commercial name: Hetrazan.
Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of diethylcarbamazine citrate.
***J.A.M.A.* 166:51 (Jan. 4) 1958.**

Preparations

Syrup Diethylcarbamazine (Hetrazan) Citrate 120 mg. per 5 ml.; pint bottles.

Tablets Diethylcarbamazine (Hetrazan) Citrate 50 mg., scored.

Heparin Sodium — Use in Hyperlipemia

The Council has reviewed and evaluated the laboratory and clinical evidence pertaining to the use of heparin (Heparin, Liquaemin) sodium as an adjunct to the management of hyperlipemia (hyperlipoidemia) associated with atherosclerosis. This agent has been extensively employed as a rapid-acting anticoagulant, and its usefulness in the management of conditions characterized by thrombosis and embolism is well established. (See the monograph on heparin sodium in New and Nonofficial Remedies.) A new and different reason for the use of heparin in hyperlipemia stemmed from the accidental observation in 1943 that the turbidity of plasma caused by alimentary lipemia disappeared completely after injection of heparin into the dog. (When heparin is added to lipemic serum in a test tube, similar clearing does not occur.) This phenomenon, later called the "lipid-clearing" effect of heparin, has now been observed in all species of laboratory animals and in man. Since a single dose of heparin will affect the blood lipids for several days but will reduce blood coagulability for only a few hours, it seems likely that the lipid-clearing effect is independent of anticoagulant activity.

It is now generally agreed that the principal effect of heparin on the blood lipids is mediated through an alteration in their physical state rather than by any significant change in total lipid concentration. Thus, plasma ultracentrifugation studies have shown that the injection of heparin causes a marked shift in the distribution of lipoproteins in human plasma; the drug rapidly converts lipoproteins of low density to lipoproteins of higher density. Some investigators feel that the lipoproteins most effected by heparin, namely, those of low density, are also the lipoproteins most likely to be found in high concentration in atherosclerosis, and indeed this high concentration is believed by some to be the cause of the sclerotic lesions. These low-density lipoproteins are also believed to contain abnormally large proportions of cholesterol, and strong evidence of an association between high concentrations of blood cholesterol and atherosclerosis has also been presented in recent years.

Hence, there are some reasons for a trial of heparin sodium as an adjunct to the management of hyperlipemia associated with atherosclerosis. The plasma ultracentrifugation studies have yielded evidence that long-term heparin therapy causes a shift in the lipoprotein pattern toward normal, and such therapy is claimed to exert a favorable influence on patients with overt manifestations of atherosclerosis. Thus early clinical trials based on this hypothesis have suggested that the weekly administration of heparin reduces the incidence of attacks of angina pectoris. These studies, however, have not as yet been confirmed.

More recently, evidence has been recorded to indicate that survival time after proved myocardial infarction is significantly increased by heparin therapy. Although these results are encouraging, much more long-term study under carefully controlled conditions is necessary to determine whether beneficial effects in postinfarction longevity are due to the influence of heparin on blood lipids or to its anticoagulant effect or to both. Moreover, the ultimate safety of such a therapeutic regimen from the point of view of subsequent hemorrhagic episodes has not been conclusively established

Although a strict cause-and-effect relationship has not been proved, there is overwhelming epidemiologic evidence that prolonged hyperlipemia is at least one factor linked with the development of atherosclerotic cardiovascular disease. Theoretically then, a sustained shift in the spectrum of circulating lipids would be desirable, both as a preventive measure before the development of symptoms and in an attempt to delay or reverse the process after symptoms have appeared. Heparin sodium has been suggested as a possible therapeutic means of attaining this end. It should be borne in mind, however, that a sizable percentage of the circulating lipids consists of esterified cholesterol and that the influence of heparin on cholesterol concentration is uncertain. For example, no significant change in serum cholesterol levels has been observed when heparin is employed to enhance survival time after myocardial infarction. Furthermore, there is no proof that heparin can effect a lipoprotein shift in patients with hypercholesterolemia but without hyperlipemia.

Since many investigators believe that cholesterol in particular, rather than lipids in general, is the blood constituent most likely to be etiologically associated with atherosclerosis, and since the effects of heparin on cholesterol are so poorly understood, considerable disagreement has arisen as to the feasibility of long-term heparin therapy. On the basis of information available to date, there is no objective evidence

that heparin can reverse or eradicate preexisting atherosclerotic conditions. Valid evidence is also lacking that heparin exerts a significant prophylactic effect, either in preventing or in delaying the onset of new disease. Hence, its clinical use as an adjunct to the management of hyperlipemia is considered experimental. On the basis of current knowledge, trial of the drug in patients with proved myocardial infarction may be justified as a possible means of increasing longevity. However, too many gaps in knowledge exist to warrant the routine use of heparin except as an anticoagulant. Only long-term clinical experience will determine its ultimate value in cardiovascular disease.

Because the dosage of heparin ordinarily used for the management of hyperlipemia is less than that used for anticoagulant effects, the possibility of bleeding episodes is appreciably reduced. Nevertheless, long-term experimental therapy with heparin in atherosclerosis should be accompanied by periodic checks on clotting time. Therapy should be terminated immediately at the first indication of abnormal bleeding tendencies. These have been encountered occasionally when heparin was being used for long periods in doses well under those ordinarily used to affect coagulation.

In view of the experimental status of heparin therapy in hyperlipemia and atherosclerosis, no well-defined minimum effective dose has been determined. The most frequently employed dosage is 200 mg. given subcutaneously twice weekly.

The Council voted to expand New and Nonofficial Drugs to describe the use of heparin sodium as an adjunct to the management of hyperlipemia associated with atherosclerosis.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of this additional use of heparin sodium.

J.A.M.A. 166:52 (Jan. 4) 1958.

Tetracycline Phosphate Complex

Panmycin® Phosphate
Sumycin®
Tetrex®

TETRACYCLINE PHOSPHATE COMPLEX is a relatively insoluble complex precipitated by the addition of a solution of sodium metaphosphate to a solution of tetracycline or its hydrochloride. The anhydrous complex contains approximately 45% carbon, 6 to 8% phosphorus, 4.8% nitrogen, 3.9% hydrogen, and 0.7 to 1.4% sodium. The structural formula of tetracycline phosphate complex has not been determined.

Actions and Uses

Tetracycline phosphate complex has the same actions and uses as the parent antibiotic, tetracycline, or its hydrochloride or calcium salts. However, the phosphate complex is more rapidly and completely absorbed from the gastrointestinal tract than is the free base or its salts and therefore produces somewhat higher blood levels after oral administration. The phosphate complex is used for the same indications as other tetracycline preparations, and the incidence and nature of side-effects appear to be identical for each. (See the monograph on tetracycline hydrochloride in New and Nonofficial Remedies.)

Dosage

Tetracycline phosphate complex is administered orally, and dosage is expressed in terms of the parent drug. For adults, the usual total dose is 1 Gm. per day given in two to four divided doses. Total daily dosage for children is 25 mg. per kilogram of body weight.

Preparations: capsules 100 mg. and 250 mg.

Applicable commercial names: Panmycin Phosphate, Sumycin, Tetrex.

Bristol Laboratories Inc. cooperated by furnishing scientific data to aid in the evaluation of tetracycline phosphate complex.

J.A.M.A. 166:52 (Jan. 4) 1958.

Preparations

Capsules Tetracycline (Panmycin) Phosphate Complex 125 mg.

Capsules Tetracycline (Panmycin; Sumycin; Tetrex) Phosphate Complex 250 mg.

Drops, Pediatric, Tetracycline (Sumycin; Tetrex) Phosphate Complex 100 mg. per ml.; 10 ml. bottles.

Suspension Tetracycline (Sumycin; Tetrex) Phosphate Complex 125 mg. per 5 ml.; 60 ml. bottles.

Bacterial Endocarditis

Current Status of Therapy of

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. KAUTZ, M.D., *Secretary.*

MAXWELL FINLAND, M.D., BOSTON

The most dramatic effects of the use of antibiotics are demonstrable in those infections which in the past had been almost invariably fatal. This is well illustrated in cases of bacterial endocarditis, for in this disease recoveries before the antibiotic era were considered to be curiosities (the authenticity of many of them remains in doubt), whereas at present the great majority (from 60 to 80% or even more) of patients whose cases are recognized recover if treated early and properly with antibiotics. The incidence of bacterial endocarditis has probably been reduced by the general use of antibiotics in the treatment or prevention of infections, including those which predispose the body to the disease, directly or indirectly. The only reliable data in this regard, however, are the over-all reduction in the occurrence of this lesion in several large series of autopsies, from an average of about 1.5% prior to 1943 to about 0.5% in more recent years.

The primary purpose of this paper is to summarize and discuss briefly the current status of the use of drugs in the definitive treatment of cases of bacterial endocarditis. Some mention of surgical procedures is also included. The clinical features of the disease are adequately described in most of the modern textbooks of medicine and therefore will be mentioned only briefly when pertinent. For a recent summary and documentation of the important features of the disease, the reader is referred to the monograph by Kerr.[1] The literature dealing with the use of antibiotics in this disease through 1953 has been reviewed and critically analyzed by Finland.[2] Other summaries of the present status of the diagnosis, treatment, and prevention have recently been presented by Bartelheimer and Engert,[3] Hunter and Paterson,[4] and Kellow and Dowling.[5]

Etiological Diagnosis

In the management of any patient known or suspected of having bacterial endocarditis, the first and major diagnostic effort should be centered on the identification of the causative organism and the determination of its susceptibility to the proper antibiotics, for the following reasons: 1. The definitive and curative treatment of bacterial endocarditis depends primarily, if not solely, on the proper choice and use of antibiotics. 2. The antibiotics owe their curative effects entirely to their action against the bacteria that cause the infection. 3. These bacteria may vary in their susceptibility to the available antibiotics. 4. The choice of the optimum agent or combination of agents, their dosage, and the duration of treatment required for the complete eradication of

From the Thorndike Memorial Laboratory, Second and Fourth (Harvard) Medical Services, Boston City Hospital, and the Department of Medicine, Harvard Medical School.

the causative organism from the endocardial lesion and from secondary lesions, therefore, depend on the identification of the causative organism and the knowledge of its sensitivity to antibiotics. 5. When the causative organism cannot be determined, the choice of therapy must be based on an intelligent guess as to the most likely one; it is then necessary to vary the treatment regimen blindly if the effects fall short of those expected. The over-all results of treatment in such cases are much less satisfactory than in those in which treatment is tailored to the organism obtained from the patient and properly identified.

From this practical point of view, cases of bacterial endocarditis may be classified into two major categories: those with positive blood cultures and those with negative blood cultures. The first category may, of course, be subdivided according to the organisms recovered from the blood and according to their susceptibility to available antibacterial agents. The frequency with which positive blood cultures are obtained in authentic cases of bacterial endocarditis may vary with the pathogenesis of the infected lesion, its physical character, its site, and the fact of whether the patient has recently received antibacterial agents. To a certain extent also, success in obtaining positive blood cultures depends on the number of cultures and on the choice of bacteriological mediums and methods. Under optimum conditions, up to 90% of cases may yield positive blood cultures. However, under some circumstances and sometimes for unexplained reasons, organisms could be recovered from the blood in only about one-third of clinically diagnosed cases even after repeated attempts. This was well illustrated in several large series of cases reported from France and Germany after World War II.[3] In most of the recent British and American series, the causative organism was recovered from the blood in about 70 to 80% of the cases of bacterial endocarditis.

By far the greatest majority of positive cultures are obtained with the use of good, versatile liquid mediums, such as are used routinely in most bacteriological laboratories. It is essential, however, to keep the blood cultures under observation for periods up to three weeks before they are discarded as negative. In patients in whom special or fastidious organisms are suspected, such as the Brucella species, various anaerobes, yeast, or fungi, appropriate mediums or methods are selected in attempts to grow them. It is best in such situations to enlist the cooperation of the bacteriologist, who, in turn, should always be aware that a specimen is from a patient suspected of having endocarditis. Positive cultures should be retained for study of the sensitivity of the organisms to any antibiotics that might be useful.

The most common causative organisms identified in the blood cultures of patients with bacterial endocarditis are streptococci of the viridans group, including both the alpha-hemolytic, or green-producing, and the gamma, or nonhemolytic varieties; together these may be found in from 75 to 85% of the positive cases. This is fortunate, for the viridans group of streptococci are all moderately or highly susceptible to penicillin; the great majority are inhibited by 0.1 unit per cubic centimeter or less, and almost all the rest are sensitive to 1 unit per cubic centimeter or less. Moreover, there is no good evidence of any general or significant increase in the resistance of these organisms to penicillin or to any of the other commonly used antibiotics. Only pneumococci, gonococci, and group A hemolytic streptococci, which are relatively infrequent causes of endocarditis, are more sensitive than streptococci of the viridans group.

Enterococci (group D streptococci), which are relatively resistant to penicillin alone, are being encountered with apparently greater frequency than in the preantibiotic period; they may now be responsible for 5 to 15% of cases. On blood agar, the various species of enterococci may resemble either Streptococcus viridans or betahemolytic streptococci and can be distinguished from either of these by their ability to survive and grow at 45° C and in mediums containing a concentration of 6.5% sodium chloride.

Micrococci (staphylococci), which include strains of Micrococcus pyogenes var. aureus and also, although to a less extent, M. pyogenes var. albus, have been gaining in prominence as a cause of bacterial endocarditis in recent years. They are of particular interest and importance because most of them are from infections acquired in hospitals and are generally resistant to penicillin and often to some, or all, of the other antibiotics that are most frequently used in those hospitals.

Almost any of a long list of other bacteria, and even yeasts and fungi, may cause endocarditis. Some of them, such as the antibiotic-resistant yeasts and fungi, have gained in prominence with the increasing use of antibiotics, whereas others, such as the pneumococci, group A hemolytic streptococci, and gonococci, all of which are highly sensitive to penicillin and to most of the other antibiotics in common use, are being encountered less frequently than in the past. In addition, almost all infections that are accompanied by bacteremia may have endocarditis as a complication, especially if untreated, or if treatment is begun late or is inadequate.

From a clinical point of view, streptococci of the viridans group are most frequently found in patients with bacterial endocarditis who have underlying rheumatic valvular heart disease or congenital lesions of the heart or great vessels. The most frequent antecedent episodes elicited in such cases are simple upper respiratory tract infections or dental manipulations, but in the majority of cases no precipitating factors can be elicited. On the other hand, endocarditis due to enterococci or coliform organisms, including Aerobacter aerogenes, Pseudomonas aeruginosa, and various species of Proteus organisms, occurs most frequently in patients with infections of the genitourinary or the intestinal tract or after various diagnostic or therapeutic procedures carried out in these regions. Micrococcic endocarditis is usually, but not always, accompanied by infection with the same organism elsewhere in the body, although this may consist of no more than a small furuncle. Micrococci are the most common organisms recovered in the endocarditis that occurs in narcotic addicts and as a complication of operations on the heart. They have recently been described after infections of veins at the site of cut-downs or of the insertion of catheters for continuous intravenous infusions. Infections with yeast or fungi, notably with Candida albicans, are also encountered in patients undergoing prolonged prophylaxis or therapy with antibiotics for other serious illnesses or infections, particularly when the antibiotics are given with corticotropin (Acthar, Corticotropin, Depo-Acth) or glucocorticoid (corticosteroid) hormones.

The prime importance of identification of the etiological agent for the management of cases of bacterial endocarditis makes it mandatory to obtain blood cultures from every patient in whom this diagnosis is made or suspected. The effort and cost of this procedure, even when repeated often, are relatively small when compared with the total cost of managing such a case and with the usefulness of the positive result in achieving the best therapeutic effect. Blood cultures should, therefore, be made in all individuals who present any of the cardinal manifestations of bacterial endocarditis. These include evidence of heart disease associated with a murmur when accompanied by persisting fever, petechiae or other embolic manifestations, enlarged spleen, gross or microscopic hematuria, mild or moderate anemia (normocytic, normochromic in type), mild clubbing of the fingers, chills, sweats, anorexia, weakness, fatigue, and loss of weight. Blood cultures should also be made in patients known to have rheumatic or congenital heart disease whenever they have unexplained fever of more than a few days' duration, particularly if there is a history of recent dental procedures. They should likewise be done in patients who have repeated chills or continuous fever after urologic or intestinal operations or diagnostic instrumentations.

At least four, but preferably more, blood cultures should be made at different times of the day and on at least two

days, except in patients who are in severe cardiac failure or have evidence of extensive embolization especially to the central nervous system, indicating the need for immediate treatment. Even in such cases, at least two or three blood cultures obtained an hour or more apart should be made before treatment is begun. Increasing the number of cultures and extending them over longer periods than two or three days yield progressively diminishing returns in percentage of additional patients from whom positive results can be expected.

Blood obtained from the antecubital vein is as satisfactory as that from any other source; arterial blood cultures are of little or no additional help. However, if the diagnostic possibilities include tuberculosis or other granulomatous diseases, tumors, or blood dyscrasias for which biopsies are done or cultures of bone marrow are made, routine cultures of the marrow for ordinary bacterial pathogens should also be included. This is true especially in patients who have recently received antibiotics. Occasionally in patients with bacterial endocarditis, positive cultures have been obtained in this way when simultaneous arterial and venous blood cultures failed to yield the organism. In patients who are receiving or have recently received antibacterial therapy, it is advisable to stop all antimicrobial treatment for a few days before taking the blood cultures, except when it is felt that the life of the patient might be jeopardized by discontinuing all suppressive therapy. The alternatives of adding inhibitory agents to the blood, such as *p*-aminobenzoic acid when sulfonamides are being used, penicillinase in patients receiving penicillin, or magnesium sulfate if one of the tetracyclines is being given, are probably of relatively little help and are much less desirable than stopping all antibacterial therapy for a period sufficient to eliminate the drugs completely. Consultations with the laboratory are helpful for the choice of special mediums when negative results are obtained in the initial attempts.

Positive results of blood cultures in patients suspected clinically of having bacterial endocarditis are usually reliable reflections of the cause of the disease. However, when the organism recovered is a common contaminant, such as M. pyogenes var. albus or Escherichia coli, or even Str. viridans, it is highly desirable to confirm this by demonstrating the same organism in at least one additional blood culture. Such confirmation is mandatory in patients in whom such common and relatively nonpathogenic organisms are recovered from routine blood cultures and in whom there is no clinical suspicion of endocarditis.

In patients who have focal or systemic infections that are frequently accompanied by bacteremia, endocarditis should be suspected when (1) the bacteremia persists for unusually long periods, (2) it recurs, particularly after the local lesion or the underlying infection appears to have cleared, (3) a cardiac murmur appears or changes in character, or (4) embolic phenomena occur in the absence of demonstrable thrombophlebitis. In such cases, the causative organism of the endocarditis is usually the same as that which caused the original infection. However, superinfections with new organisms may occur, particularly in patients who have received adequate treatment with antibacterial agents that can be depended on to eliminate the original infection.

Tests for Susceptibility

The isolation and identification of the causative organisms in cases of bacterial endocarditis may be helpful clinically in delineating some possible predisposing factors and may thus serve as a practical aid in the management of some cases and in the prognosis of most cases. However, as already indicated, the primary and most useful purpose of these procedures is for the choice and conduct of specific antibacterial therapy. It follows that the determination of the susceptibility of the organism to any of the available agents may be equally essential, but this is true only within certain limits. In general, quantitative tests done by a serial dilution method in broth or on agar are to be preferred over the disk method, and cultures should be saved for that purpose even after the organisms have been tested routinely and a qualitative result has been obtained by the latter method. The tube-dilution method, however, is useful primarily for testing the penicillin susceptibility of streptococci of the viridans group or enterococci, since penicillin is the only antibiotic that may be given over a wide range of dosage. It may also be useful in micrococcic endocarditis. All the other antibiotics can be used only within a limited range and, for endocarditis, are generally given in about the maximum tolerated dose.

The results of sensitivity tests are also helpful only when they are performed on organisms that are known to vary in their susceptibility to individual antibiotics or to different antibiotics and when such differences are crucial in the choice of the optimum agent and dosage regimen. This is true of streptococci of the viridans group, of enterococci, and of micrococci, and these, as already noted, are the most frequent causative agents encountered. The tests are not helpful and need not be done if pneumococci, group A hemolytic streptococci, or gonococci are involved, for these are uniformly and highly susceptible to penicillin, which is the agent of choice, and also to any of the other antibiotics that might be used alternatively.

If tetracycline is used in the test, it is superfluous to include its two congeners, chlortetracycline and oxytetracycline, since for practical purposes the results and their interpretation would be the same. Likewise, only erythromycin need be used and the other erythromycin-like agents, carbomycin, oleandomycin, and spiramycin, omitted, since they are generally less active against the same organism, particularly if it is a micrococcus. Their use in cases of bacterial endocarditis has not given favorable results, and, therefore, is not recommended even in infections due to erythromycin-resistant strains that may appear to be somewhat sensitive to them in vitro.

Hunter[4] has emphasized the importance of determining the bactericidal concentration of antibiotic agents individually and in certain combinations. He has also demonstrated the value of streptomycin in rendering penicillin bactericidal and in increasing the rate of killing of enterococci and of occasional strains of Str. viridans. The available methods are not suitable for routine hospital laboratories and therefore are not generally used. Simpler methods for predicting the combined action of pairs of antibiotics are available and more feasible. The simplest of these is the use of antibiotic-impregnated strips placed at right angles to each other on the surface of inoculated agar plates and observing the inhibitory action of the antibiotics at the inner angle.[6]

Choice of Antibiotic and Dosage

When the causative organism in a case of endocarditis has been identified and its sensitivity to the available antibiotics determined, the choice of the agent and dosage to be used will depend only in part on these findings. The results of recorded experiences in the use of different antibotics, as summarized in the reviews mentioned,[7] are also utilized. From the available data the following broad generalizations may be made.

1. Penicillin is the agent of choice for all cases in which the causative organisms are highly or moderately sensitive to it; these include all streptococci, pneumococci, gonococci, and micrococci. However, contrary to the experience and opinion expressed by some observers,[8] I have not found penicillin in any feasible dosage to be of any value, alone or when combined with other antibiotics, in micrococcic infections when the organism is moderately or highly resistant. Moreover, there are good reasons for avoiding the use of penicillin in such cases, not only because it is not likely to be of value when used alone but also because it may actually

decrease the effectiveness of other antibiotics to which the organisms were originally sensitive.

2. Streptomycin should be used in addition to penicillin for infections with any of the enterococci or with streptococci of the viridans group that required 0.2 unit per cubic centimeter or more of penicillin to inhibit them.

3. None of the tetracyclines or chloramphenicol should be used alone in the treatment of endocarditis caused by gram-positive organisms, even when such organisms are moderately or even highly sensitive in vitro. Such use has only infrequently resulted in cures. Although these antibiotics generally produce marked inhibition of the infection, with clinical improvement and negative blood cultures even during long periods of continuous treatment, in the majority of such cases bacteremia and symptoms generally recur soon after this treatment is stopped. The same may not be equally true in the treatment of infections with highly susceptible gram-negative bacilli, but it is best in such cases to combine one of these broad-spectrum antibiotics with streptomycin or polymyxin B when the organisms are also susceptible to these agents.

4. Streptomycin, erythromycin, the other erythromycin-like antibiotics (carbomycin, oleandomycin, spiramycin), or novobiocin should never be used alone in the treatment of bacterial endocarditis, even when the causative organism is originally highly sensitive in vitro, because of the marked tendency of the organisms to become resistant to these agents during treatment. This often happens quite rapidly even after apparent initial clinical and bacteriological improvement. In such cases the symptoms reappear, bacteremia recurs, and further treatment with the same agent is futile. Moreover, under such conditions these agents are no longer useful in any combined action with other antibiotics.

5. Combinations of erythromycin or novobiocin with streptomycin or of any of these three agents with bacitracin or with one of the broad-spectrum antibiotics may be used, provided that the causative organism is still at least moderately susceptible to each component before the combination is started.

6. None of the currently available agents in the erythromycin group other than erythromycin itself can be recommended in the treatment of endocarditis, even when the organism appears to be susceptible in vitro. Their activity is inadequate and is generally inferior to that of erythromycin, and they have not been shown to be effective even in combinations with other agents for the treatment of endocarditis.

7. In the treatment of endocarditis due to Ps. aeruginosa, polymyxin B is the drug of choice (except when severe renal damage is present), used preferably in combination with another agent to which the organism is still sensitive. Polymyxin B may also be used in the same manner in infections caused by other susceptible gram-negative bacilli, particularly A. aerogenes, but not when a strain of Proteus organisms is involved.

8. Bacitracin is a useful agent in the treatment of penicillin-resistant micrococci infection, especially when combined with erythromycin, novobiocin, one of the tetracyclines, or chloramphenicol, provided that the organism is also sensitive to these agents and renal function is not already impaired.

9. Sulfonamides are of little, if any, use in the treatment of bacterial endocarditis when they are used alone. There are no reliable data indicating that they serve any useful purpose in combination with other antibacterial drugs, except in cases of meningococcic infections.

10. Except for penicillin, which is discussed separately, all antibiotics are given whenever possible in the maximum tolerated doses, at least at the start and for the first two or three weeks. When proper dosage forms are available, the parenteral route is preferred in all severely ill patients, at least during the first few days and until the clinical condition of the patient is much improved. The following optimum daily doses for the different antibiotics are the same regardless of whether they are used separately or in combinations.

Streptomycin.—The dosage of streptomycin, usually given as the sulfate, is 2 Gm. intramuscularly; 3 or even 4 Gm. daily may be used for the first three or four days in serious infections with susceptible gram-negative organisms. Streptomycin is preferred over dihydrostreptomycin because the toxic effects are less severe. The 1:1 mixture of the two has been suggested as likely to reduce the toxicity of each, but reported results are not uniform in this regard.[9]

Tetracycline, Chlortetracycline, or Oxytetracycline.—The dosage of tetracycline (Achromycin, Panmycin, Polycycline, Tetracyn), of chlortetracycline (Aureomycin), or of oxytetracycline (Terramycin), given as the hydrochloride, is 2 Gm. orally or 1 Gm. intravenously. Twice these doses may be used during the first three to seven days.

Chloramphenicol.—The dosage of chloramphenicol (Chloromycetin) is 4 Gm. orally or 2 Gm. intravenously or intramuscularly; 3 Gm. is given orally after the first few days.

Erythromycin.—The dosage of erythromycin (Erythrocin, Erythromycin, Ilotycin), given either as the base or the stearate, is 3 Gm. orally or, given as the glucoheptonate or lactobionate, 1.5 Gm. intravenously during the first week. The dose is 2 Gm. orally or 1 Gm. intravenously thereafter.

Novobiocin.—The dosage of novobiocin (Albamycin, Cathomycin), usually given as the sodium salt, is at first 3 Gm. orally then 2 Gm. The intravenous dose is 2 Gm. for two to five days, then 1 Gm.

Bacitracin.—The dosage of bacitracin is 100,000 units given intramuscularly.

Polymyxin B.—The dosage of polymyxin B (Aerosporin, Polymyxin B), given as the sulfate, is 2.5 mg. per kilogram of body weight, administered intramuscularly. A total of not more than 200 mg. is given initially, then 1.5 or 2 mg. per kilogram of body weight.

Neomycin.—The dosage of neomycin (Mycifradin, Neomycin), given as the sulfate, is 500 mg. intramuscularly for no longer than one or two weeks. Neomycin is used only in desperation when it is highly active in vitro against organisms resistant to other antibiotics. Irreversible deafness and reversible renal damage may be expected even with this dosage.

Penicillin.—The optimum dosage of penicillin required to cure endocarditis probably varies not only with the in vitro sensitivity of the causative organism but also with the character and age of the endocardial and other lesions, with the particular form used and the manner in which it is administered, and with other factors that cannot be determined.[2] The additional use of streptomycin also reduces the daily dose of penicillin required and the time over which these agents must be given. Although the value of this combined action of penicillin and streptomycin has been clearly demonstrated for enterococcic infections and only infrequently for other streptococci, the combined treatment is now also generally used in infections due to streptococci of the viridans group. The use of probenecid (Benemid) in oral doses of 2 Gm. daily (500 mg. every six hours) produces on the average a twofold increase in the blood levels that are attained and maintained with any given dose of penicillin by any route and in any systemic form. This, therefore, permits a corresponding reduction in the amount of penicillin that must be given. Probenecid does not have any effect on the blood levels produced by any other antibiotics.

The sodium or potassium salt of penicillin G intramuscularly is preferred for penicillin in the treatment of endocarditis; the reasons for this are set forth in detail elsewhere.[2] This method may not be feasible when it becomes necessary to give very large doses of penicillin, such as have been recommended in the treatment of enterococcic or micrococcic endocarditis in which the organisms are only slightly sensitive. However, up to 8 million or 12 million units daily (1 million units every two or three hours) can be given in this manner for as long as two or three weeks if necessary. Many experienced clinicians

prefer to give these dosages, particularly the larger amounts, by a constant intravenous drip through a polyethylene tube inserted into a vein and kept patent by the inclusion of a concentration of heparin (Heparin, Liquaemin) sodium just adequate to prevent local thrombosis. Others have recommended the intramuscular use of procaine penicillin G, since this is much less irritating locally than the soluble salts; it does not provide the high peak levels, however, which are desirable and which are best attained with the latter. When procaine penicillin G is given, only the aqueous suspension should be used; even with this form the total amount that can be injected daily falls short of the large amounts that may be required in some cases. Benzathine penicillin G (Bicillin, Permapen) has no place in the treatment of bacterial endocarditis.

It has recently been demonstrated that patients with endocarditis due to sensitive streptococci can be treated successfully by the oral use of phenoxymethyl penicillin (penicillin V) (Pen-Vee, V-Cillin).[10] This method is not recommended, however, because the risk of omitting doses is great, because uniform, predictable absorption cannot be assured, and because gastrointestinal irritation may occur, as with other antibiotics, when amounts in excess of 3 or 4 Gm. (4,800,000 to 6,400,000 units) are given daily.

Nichols, Richards, and Finland[11] have recently utilized a penicillin regimen that is better tolerated, is less difficult to carry out, and offers both persistently high levels and intermittent peaks that are much higher and more nearly approach the levels desired in enterococcic infections. In this regimen, the aqueous suspension of procaine penicillin G is given intramuscularly in doses of 1,200,000 units every six hours; probenecid is given orally every six hours, and intravenous injections of 1 million units (or larger amounts) of sodium or potassium penicillin G are given in a convenient volume of saline or 5% dextrose solution (20 or 30 cc.) out of a syringe three or four times daily between the intramuscular doses. By the reasoning offered elsewhere,[2] this method should be preferred over constant intravenous injections.

A recent survey made by Hunter and Paterson[4] among 23 investigators indicated that treatment of endocarditis due to penicillin-sensitive streptococci (of the viridans group) has been carried out successfully in two weeks with a dose of penicillin ranging from 2 million to 12 million units, plus about 2 Gm. of streptomycin, daily. Among 146 patients so treated, only 8 (or 6%) relapsed clinically or bacteriologically, a rate that compares favorably with that obtained when longer periods of treatment were used. In this survey, 10 of the 146 strains were resistant to 0.25 or 0.5 unit, and the rest were sensitive to 0.1 unit per cubic centimeter or less of penicillin. These authors classified the occasional organisms that require 0.2 to 2 units per cubic centimeter as intermediate in susceptibility between the sensitive varieties of Str. viridans and the resistant enterococci and recommended that in the management of cases due to such organisms the dosage should be the same as that for enterococci.

Kellow and Dowling[5] recommended dosage regimens which they found to be suitable in the management of the common bacteriological types of endocarditis. Some of these can be accepted with reservations. For example, a treatment period of only 10 days is recommended as adequate for infections with streptococci that are sensitive to 0.5 unit per cubic centimeter or less of penicillin. It is probably more prudent and more in accord with our experience to accept the recommendations of Hunter and Paterson in this regard and offer a minimum treatment period of two weeks, limit this to infections with organisms that are sensitive to 0.1 unit or less, and give more and longer treatment for those with less sensitive strains. Also, although tetracycline or chloramphenicol alone may be used succcessfully in the treatment of an occasional case of penicillin-resistant micrococcic endocarditis, these agents alone cannot be recommended as useful or desirable in such cases even when the organism is sensitive. Each of these agents is better used in combination with another potent antimicrococcic antibiotic, namely, erythromycin or novobiocin, provided that the micrococcus is sensitive to them also. Bacitracin or streptomycin is also useful in combination with each of the latter antibiotics. Since penicillin-resistant micrococcic endocarditis is notoriously difficult to treat and still has a mortality of 50% or higher in most clinics and under intensive treatment, only optimum therapy should be used in such cases.

It seems only reasonable and wise that any recommendations for the treatment of so serious a disease as endocarditis, regardless of its cause, should be aimed at the optimum results in the greatest number of cases, despite the increased cost and discomfort to many. This seems better than to attempt to approach the minimum effective therapy; any reduction from the optimum to approach such minimum should be considered only when it becomes necessary to compromise because the optimum dosage is not feasible or cannot be tolerated by a particular patient. The following programs of therapy are therefore offered as suggestions based on this point of view.

Recommended Programs for Antibiotic Therapy in Most Frequent Types of Bacterial Endocarditis

The most common forms of endocarditis are those due to streptococci or to micrococci, and these will be considered first.

Streptococcic Endocarditis.—Streptococci of the viridans group sensitive to 0.1 unit per cubic centimeter or less of penicillin: The dosage of penicillin is 600,000 units given intramuscularly every 6 hours, plus 1 Gm. of streptomycin every 12 hours, for seven days, then once daily for seven days.

Streptococci of the viridans group requiring 0.2 unit per cubic centimeter or more of penicillin: The dosage of penicillin is 1 million units given intramuscularly every 2 or 3 hours for two or three weeks, then every 6 hours for three or four weeks, plus 1 Gm. of streptomycin every 12 hours for two or three weeks, then every 12 hours for three or four weeks. The larger dose and longer treatment are used when the organism requires more than 1 unit per cubic centimeter or penicillin. A dosage of 500 mg. of probenecid given orally every six hours is added to enhance the levels or when the optimum dose is not well tolerated and it is necessary to give smaller or fewer doses of penicillin.

Enterococci: The dosage of penicillin varies with the susceptibility of the organism to that antibiotic; the minimum is 1 million units given intramuscularly every two or three hours. Larger amounts, up to 20 million units or more daily, may be given by constant intravenous infusion and continued for a total of six weeks. A dosage of 500 mg. of probenecid given orally every six hours for six weeks is used in all cases. Penicillin must be combined with 1 Gm. of streptomycin every 12 hours for the first three weeks, then once daily for three weeks. A combination of erythromycin with streptomycin or with bacitracin may be used as alternative therapy.

Micrococcic Endocarditis.—Organisms of M. pyogenes var. aureus or M. pyogenes var. albus sensitive to 1 unit per cubic centimeter or less of penicillin: The dosage of penicillin is 1 million units given intramuscularly every two or three hours, plus 500 mg. of probenecid given orally every six hours, for six weeks.

Micrococci resistant to 1 unit per cubic centimeter of penicillin: Two antibiotics should always be used simultaneously, and the causative organism must be moderately or highly sensitive to both before therapy is started. Preferred combinations are (1) erythromycin plus either bacitracin, streptomycin, chloramphenicol, or one of the tetracyclines, (2) novobiocin plus bacitracin, streptomycin, or a tetracycline (or possibly chloramphenicol, although

data on this combination are lacking), or (3) chloramphenicol plus bacitracin or streptomycin. Each antibitoic is given in the maximum tolerated doses as outlined previously. For the first three to seven days, the parenteral route is employed to initiate treatment. A change to oral therapy and reduction in dosage are permitted only after bacteremia, fever, and acute systemic symptoms have subsided or because the patient has developed a tolerance. The dosage should then be as large as tolerated, or the antibiotics are changed. Treatment is continued for six weeks.

Endocarditis Due to Other Organisms.—Reliance is placed more heavily on the actual sensitivity of the causative organism, as determined in vitro, or on its probable sensitivity, as gathered from available data. Thus, when group A hemolytic streptococci, pneumococci, or gonococci are the infecting organisms, these organisms may be presumed to be highly sensitive to penicillin, and it should be possible to eradicate these organisms with moderate doses of penicillin alone given over a relatively short period. A dose of 500,000 or 600,000 units of penicillin should be given intramuscularly every six hours. Treatment should be continued for three weeks because of the possibility, in the case of hemolytic streptococcic and pneumococcic infections, that there are also other foci of infection to be eradicated.

Experience with antibiotic treatment of endocarditis with uncommon organisms is limited, and any suggested regimen must be considered with that in mind. This is true, for example, even for meningococcic endocarditis. However, since the meningococcus is highly sensitive to sulfonamides, which are generally considered the agents of choice in infections with this organism, and since a meningeal focus frequently coexists in cases of meningococcic endocarditis, Kellow and Dowling[5] recommended combined sulfonamide and penicillin therapy. This procedure is designed to treat both the endocardial and the meningeal infection. A sulfonamide, preferably sulfadiazine or the triple combination, trisulfapyrimidines (rather than the less active sulfisoxazole), is given in full doses (initial dose of 4 Gm. orally or parenterally and then 1 Gm. orally every four hours), plus 1 million units of penicillin given intramuscularly every two hours. This is continued for the first two or three days, after which the penicillin is given every three or four hours for the next four or five days, and procaine penicillin G may then be given twice daily for two weeks longer.

In the treatment of endocarditis due to organisms other than those already mentioned, great reliance is placed on the use of antibiotics in combination, each being used for its own contribution or as an aid in delaying or preventing the emergence of resistance to the other members of the combination. It should be reemphasized that only antibiotics to which the organism is susceptible to some extent should be used in any combinations.

With respect to the action of antibiotics in combinations, Jawetz and Gunnison[12] have classified the antibiotics into two groups. Those of group 1, (penicillin, streptomycin, bacitracin, and neomycin) are generally bactericidal, but under certain circumstances their action may be antagonized by antibiotics of group 2 (the tetracyclines, chloramphenicol, the erythromycin group, and novobiocin) which are only bacteriostatic in their action. However, such antagonism has not been demonstrated clinically except under the special circumstances of dosage in the use of the combination of chlortetracycline and penicillin for the treatment of pneumococcic meningitis. This possible antagonism probably should not be a consideration in the choice of antibiotics used in combination in the treatment of bacterial endocarditis. Instead, each agent should be used essentially in full doses and for its special contribution as already emphasized.

In the treatment of brucella endocarditis, for example, the combination of a tetracycline with streptomycin given for a period of six weeks is the treatment of choice. The tetracycline is given orally in doses of 2 Gm. daily and the streptomycin in doses of 1 Gm. every 12 hours for two weeks, then every 24 hours for four more weeks If tolerated, a daily dose of 3 or 4 Gm. of tetracycline may be used during the first two weeks. In the event of endocarditis due to strains of Hemophilus organisms (either H. influenzae or H. parainfluenzae), it is desirable to use a combination of streptomycin with either chloramphenicol or one of the tetracyclines.

Salmonella infections, in general, do not respond satisfactorily to any form of antibiotic therapy. Chloramphenicol, which is usually the drug of choice, should be given in doses of 4 Gm. daily for two weeks and 2 or, preferably, 3 Gm. daily for four more weeks, so long as these doses are tolerated. However, in endocarditis and other focal infections or suppurating lesions due to Salmonella organisms, the tetracyclines in similar doses may be equally effective; in some patients who have previously received chloramphenicol for long periods, the tetracyclines may be preferred. The possibility of using both of the agents for their additive effects or either of them with polymyxin B may also be considered and indeed may be preferred; they are then used in equal amounts to provide the same or slightly larger total daily dose. A synergistic action of chloramphenicol with polymyxin B has been demonstrated in vitro.[13]

Combinations of streptomycin or polymyxin B with chloramphenicol or a tetracycline are also recommended for use in the treatment of endocarditis due to various other coliform organisms, particularly Aerobacter infections; however, polymyxin B is the agent of choice in infections with Ps. aeruginosa but should not be used for infections with Proteus organisms since they are not susceptible to polymyxin B.

Endocarditis in Patients with Negative Blood Cultures.—Treatment of patients with negative blood cultures is based on the probability that the endocarditis is caused by one of the common types of organisms. However, because of the uniformly greater mortality reported by most observers in such patients, as compared with the usual patients from whom the organism is recovered, and because of the greater tendency of such patients to develop cardiac failure, they are treated intensively. The regimen recommended to start treatment is the same as that in which streptococci of intermediate susceptibility are found (0.2 unit per cubic centimeter or more penicillin); if the response appears inadequate after four to seven days, the regimen recommended for enterococcic endocarditis is used.

For most of the types of cases considered, a treatment period of six weeks, has been recommended. The shorter period, namely, two weeks for subacute bacterial endocarditis due to sensitive streptococci of the viridans type, is based on accumulated experience of many observers. Treatment for three weeks for acute bacterial endocarditis due to group A hemolytic streptococci, pneumococci, gonococci, and meningococci has been recommended, but this is arbitrary and is based only on deduction from the nature of the lesion and expected response. In general, the short periods of treatment are permitted only when the organisms are highly susceptible to the antibiotics used and when the response to treatment, both clinical and bacteriological, is rapid and appears to be complete. Contrariwise, treatment may profitably be extended even beyond the six weeks when (1) the organism is only slightly sensitive or moderately resistant, (2) bacteremia persists during the first days of therapy, (3) fever and symptoms subside only gradually over a period longer than a week or 10 days, (4) the dose of antibiotic must be curtailed or interrupted, or the antibiotic temporarily discontinued or changed because of intolerance, or (5) there are large or extensive focal areas of suppuration. An additional week or two of treatment in such cases may increase the chances for cure and reduce the possibility of relapses.

Prophylaxis

Bacteremia with streptococci of the viridans group can be demonstrated with considerable frequency during various

dental manipulations. Invasion of the blood stream with enterococci or with various coliform organisms occurs frequently during or soon after instrumentation or operations on the infected genitourinary or intestinal tract. These facts, coupled with the history of such procedures antedating the onset of infection in a large proportion of patients with bacterial endocarditis, strongly suggest that measures directed at preventing such bacteremias or aimed at eliminating the organisms from the blood stream as rapidly as possible are highly desirable and may prevent the development of endocarditis under such cricumstances.

The only available method to accomplish this, other than the obvious one of attempting to minimize trauma to tissues during these procedures, is by the use of antibiotics. Since endocarditis due to the types of organisms found in the mouth affects primarily persons with valvular or congenital cardiac lesions, prophylaxis during dental manipulations is indicated principally, or only, in such individuals. Endocarditis caused by enterococci or other enteric organisms, on the other hand, may occur in apparently normal valves, so that prophylaxis would seem to be indicated after manipulations of the infected genitourinary or intestinal tract in all patients. However, there are no data from any large body of controlled experience upon which one may base any reasonable recommendation as to the choice of antibacterial agents, the dosage, or the time and duration of treatment, in relation to these procedures.

The only reasonable assumptions upon which recommendations can be based are that manipulations in the oral cavity would be associated with invasion by relatively sensitive streptococci of the viridans group and that bacteremia resulting from operations or instrumentation on the genitourinary or the intestinal tract would be associated with organisms of the common intestinal flora or those commonly found in infections of the urinary tract. In patients who are already under treatment with antibiotics or have had treatment very recently, the flora may be expected to consist of organisms that are moderately or highly resistant to the antibiotics which were being used. In any event, eradication of organisms from the circulating blood before they have become implanted should be possible with the use of the appropriate antibiotics in relatively lower doses and in a much briefer period than when endocarditis is already established. The possibility of sequestration and possible protection of the organisms from circulating antibiotics inside of phagocytic cells, however, must also be considered.

On the basis of these considerations, the following recommendations for prophylaxis seem reasonable. In patients with known valvular or congenital cardiac lesions undergoing dental manipulations, a single intramuscular dose of 600,000 units of aqueous procaine penicillin G, plus 200,000 units of sodium penicillin G or potassium penicillin G, should be given just prior to the procedure. This is provided in a single injection of 2 cc. of formulations that are available commercially. A dose of 500 mg. or 1 Gm. of streptomycin may also be added as an additional factor of safety, especially in patients who have had rheumatic fever and are receiving penicillin prophylaxis. Attempts to sterilize the dental field prior to extractions or other procedures by prolonged and intensive treatment have little, if any, likelihood of any lasting success. On the other hand, such therapy may offer an opportunity for invasion by organisms that are highly resistant to the agents used for the prophylaxis and would thus defeat its purpose. However, mixtures of bacitracin and neomycin in troches may be useful after dental procedures, although the actual value of their use is not known. They have possible merit in that there are not likely to be any important pathogenic organisms resistant to these agents in the mouth and these antibiotics would not ordinarily be selected for systemic use should infection occur. Recent revival of interest in extraction of all teeeth in patients with valvular or congenital heart disease seems rather drastic. Except in those in whom most of the teeth are carious and there is extensive periodontal sepsis, it does not seem warranted as a routine procedure on the basis of the small amount of data available.

A prophylaxis regimen for use during genitourinary or intestinal procedures is more difficult to formulate. For anticipated invasion by enterococci, a combination of penicillin plus streptomycin seems reasonable. This may be of value also against streptomycin-sensitive coliforms but would be inadequate against most gram-negative bacilli, particularly Pseudomonas, Proteus, or Aerobacter organisms. The addition of chloramphenicol or tetracycline to this combination may therefore be suggested. Treatment with this triple combination is best started within 1 or 2 hours of the procedure and continued over a period of 24 to 48 hours.

Other Forms of Therapy

Operations for the correction of patent ductus arteriosus have proved successful in preventing the occurrence of infections or reinfections at this site. The appropriate operation is therefore recommended in such cases even after the patient has been cured of an attack of endocarditis.

Although most emboli in cases of bacterial endocarditis due to streptococci of the viridans group may be expected to resolve spontaneously, embolectomy should be done promptly in other cases or whenever a large embolus is involved. Excision or ligation of infected arteriovenous fistulas and of accessible mycotic aneurysms should be done during the antibiotic treatment. This procedure may increase the number of permanent cures in certain types of apparently resistant cases.

Rupture of an infarcted and infected spleen and persistence of infection within splenic abscesses even after apparent cure of the endocardial lesion have proved to be the cause of death or a contributing factor in failures of therapy in some cases. Splenectomy may, therefore, be lifesaving in some patients in whom large infarcts or abscesses of the spleen are suspected; this operation should be carried out in such cases during the last week or two of the antibiotic therapy.

The use of anticoagulants has been recommended as a means of increasing the efficacy of the antibacterial therapy of endocarditis. These agents were used by several clinicians in a number of cases during the sulfonamide era and when penicillin was first introduced. Heparin sodium was the agent of choice, primarily because its effects could promptly be neutralized in the event of hemorrhage. However, experience with this treatment was not encouraging, and its use proved to be most dangerous in exactly those patients for whom it was expected to be most beneficial, namely, those with large and multiple emboli. Subarachnoid hemorrhage occurred with alarming frequency in these patients during heparinization and was almost invariably fatal before the curative effect of the antibacterial agent could be achieved. This form of therapy has, therefore, been abandoned.

The use of the anti-inflammatory glucocorticoids or corticotropin has been recommended as an adjunct to the antibiotic therapy of bacterial endocarditis, particularly by French clinicians. There is no evidence to indicate that any of the alleged benefits have actually been derived from their use, except perhaps for the symptomatic relief offered in those patients in whom the bacterial endocarditis accompanies active acute rheumatic fever. However, because of the adverse systemic effects of the prolonged use of these hormones when given in the doses required to produce and sustain the anti-inflammatory effect, and because of the possibility of superinfections with other resistant bacteria, the use of these hormones cannot be recommended in cases of active bacterial endocarditis.

Prognosis

The cure rate in cases that are adequately treated is dependent on the infecting organisms, on its response to the treatment used, and, to a large extent, on the amount and

nature of the damage already done when treatment is started. An over-all cure rate of about 70% can be expected. However, up to 90% cures or more can be achieved in patients with infection due to the common, penicillin-sensitive streptococci when treatment is begun early. On the other hand, the treatment of micrococcic endocarditis has been successful in only about one-half of the cases. Recent experiences with infections due to antibiotic-resistant organisms and arising in hospitals have been even less favorable.

Relapses of the infection usually occur during the first few weeks after treatment is stopped; in such cases, retreatment at a higher dosage and for a longer period is indicated and is often successful. Reinfections may occur at any time, however, and are then treated the same as the original infections. In occasional patients, showers of petechiae or minor embolic episodes occur in the absence of demonstrable bacteremia or other evidence of infection for several weeks after apparent cure. No treatment is indicated in such patients; but they require careful study and observation to rule out relapse or reinfection.

Congestive heart-failure may occur, not only as part of the active disease, but it may begin or increase as a result of the healing process after the infection has been eliminated. Anticipation and proper management of this complication are therefore important, particularly when the patient first begins to ambulate. Most of the deaths that occur in patients after the infection has been cured are due to congestive cardiac failure. Occasionally, in patients in whom treatment is begun late in the disease, renal failure may occur and is associated with a lesion that is indistinguishable from chronic glomerulonephritis, morphologically and clinically.

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MEETING DATES 1958

April

Association of Western Hospitals
Includes Hospital Pharmacy Section—April 21-24, San Francisco, Calif. Civic Auditorium; St. Francis Hotel

American Pharmaceutical Association
Convention—April 20-26, Los Angeles, Calif. Hotel Biltmore

American Society of Hospital Pharmacists
Annual Meeting—April 20-22, Los Angeles, Calif. Hotel Biltmore

Tri-State Hospital Assembly
Includes Hospital Pharmacy Section—April 28-30, Chicago, Ill. Palmer House

May

National Hospital Week—May 11-17

Southeastern Hospital Conference
Includes Meeting of Southeastern Society of Hospital Pharmacists—May 14-16, Miami Beach, Fla. Hotel Fountainbleau

June

Institute on Hospital Pharmacy (A.H.A.)
June 16-20, Philadelphia, Pa. Temple University Campus

Catholic Hospital Association
Annual Convention—June 21-26, Atlantic City, N. J. Convention Hall; Dennis Hotel

Institute for Hospital Pharmacists (C.H.A.)
June 21-24, Atlantic City, N.J.

July

Philadelphia College of Pharmacy and Science Summer Courses
July 7-August 1, Philadelphia, Pa.

Preparation of Parenteral Products
July 7-18, Fifth Annual Radiochemical Institute

Principles of Radioactivity and Measurement
July 7-18

Biological and Medical Application
July 21-25

Radiochemical Instrumentation
July 28-August 1

Institute on Hospital Pharmacy (A.H.A.)
Chicago—July 28-August 1. University of Chicago

August

American Hospital Association —
Annual Convention—August 18-21, Chicago, Ill. International Amphitheatre; Palmer House

September

International Pharmaceutical Federation
September 8-13, Brussels, Belgium

POSITIONS

in hospital pharmacy

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PHARMACIST—female; experienced in both hospital and retail pharmacy. Prefer Southwest or Mid-Atlantic area. PW-11.

CHIEF PHARMACIST—prefer general hospital in Florida; registered in Ohio and Florida; experienced in both hospital and retail pharmacy. PW-12.

CHIEF PHARMACIST—or assistant chief pharmacist at large hospital; prefer St. Louis vicinity; presently employed as staff pharmacist in hospital; registered in Missouri. PW-13.

CHIEF PHARMACIST—prefer Minnesota or California, with registration in those states; ten years' experience with government service, including commissions in U. S. Public Health Service and in the Navy; experience with the Veterans' Administration as Chief Pharmacist; Pharm. D. degree. PW-15.

PHARMACIST—New Jersey registration; prefer Pennsylvania, Florida, D. C., or Virginia; experienced in managing retail pharmacy. PW-18.

CHIEF PHARMACIST—or chief pharmacist—purchasing agent; prefer non-sectarian and non-governmental institution of 200-bed capacity or larger; experienced in managing retail and hospital pharmacy. PW-19.

CHIEF PHARMACIST—prefer teaching hospital—registered in Indiana, Michigan and Missouri; prefer general hospital in Midwest; experienced in teaching and in hospital pharmacy. PW-26.

STAFF PHARMACIST—prefer Chicago vicinity; registered in Illinois; graduate of the University of Illinois, College of Pharmacy. PW-31.

CHIEF PHARMACIST—or assistant chief pharmacist in medium size hospital; registered in Indiana, Michigan and Wisconsin; six years' experience as chief pharmacist; experienced as pharmacist-purchasing agent; two years as such; prefer Midwest or East. PW-32.

STAFF PHARMACIST—graduate, Masssachusetts College of Pharmacy; age 27; registered in Massachusetts and New Hampshire; four years' experience before registration and four years in store with large prescription volume. PW-35.

CHIEF PHARMACIST—or assistant chief pharmacist; M. S. in hospital pharmacy; internship; available after February, 1958. PW-36.

STAFF PHARMACIST—graduate of Howard University, 1957; age 24, male; D. C. registration. PW-43.

PHARMACIST—graduate of Medical College of Virginia; age 26; served two years in Marine Corps; managerial experience. PW-45.

HOSPITAL PHARMACY INTERN—graduate of the University of Washington College of Pharmacy; age 25; completed military requirements; prefer Northwest. PW-46.

PHARMACIST—graduate of Wayne University College of Pharmacy; hospital experience; prefer D. C. area. PW-49.

STAFF PHARMACIST—graduate Howard University College of Pharmacy in 1957; age 31; limited experience but anxious to learn; any location. PW-50.

STAFF PHARMACIST—or assistant chief pharmacist; graduate George Washington University College of Pharmacy; prefer D. C. or Florida area; registered in D. C. PW-52.

CHIEF PHARMACIST—300 plus bed hospital preferred; completed hospital pharmacy internship at Jefferson Medical College hospital; registered in Pennsylvania and Texas; age 25; male; completed service requirements. PW-55.

STAFF PHARMACIST—desires position in Eastern Pennsylvania; graduate of Philadelphia College of Pharmacy; two years' graduate study at Northwestern University; three years' experience at University of Chicago Clinics; single male. PW-57.

CHIEF PHARMACIST—any location; M.S. degree in hospital pharmacy from the University of Michigan; completed service requirements; single, male, age 29. PW-59.

CHIEF PHARMACIST—prefer middle West; registered in Illinois; female, single; graduate of University of Illinois College of Pharmacy; presently employed as Chief Pharmacist. PW-61.

CHIEF PHARMACIST—M. S. Degree in hospital pharmacy; prefer East; male, single; extensive experience, including pharmacy and administrative officer in Air Force. PW-62.

STAFF PHARMACIST—completed military requirements; experienced in hospital pharmacy; prefer mid-Atlantic area; single, male. PW-63.

CHIEF PHARMACIST—registered in Tennessee, Louisiana and Texas; prefer South; graduate of University of Tennessee School of Pharmacy; also attended Louisiana State University. PW-64.

PHARMACIST—desires position Baltimore area; prefer small hospital; experience includes 21 years as owner-manager of retail store. PW-65.

STAFF PHARMACIST—registered in Pennsylvania; graduate of Duquesne University; prefer location in large city but in any section of the country; single, female; PW-67.

INDIAN PHARMACIST—desires appointment to obtain higher training in hospital pharmacy; graduate Madras University; 1½ years' experience in 1,000 bed hospital, including inpatient and outpatient dispensing, parenteral and general manufacturing, and administration; available September, 1958. PW-68.

CHIEF PHARMACIST—M. S. degree in hospital pharmacy; served residency at V A Center in Los Angeles; 3 years' experience as chief pharmacist in V. A. since that time; registered in Kentucky and Florida; prefer Midwest location. PW-69.

positions open

STAFF PHARMACIST—registered in Illinois; for manufacturing or dispensing in large teaching hospital; excellent equipment; good hours; two weeks' vacation; sick leave; minimum starting salary, $470.00 per month; higher salary for those experienced in manufacturing. PO-1.

CHIEF PHARMACIST—650 bed hospital, the largest voluntary hospital specializing in the treatment of long-term illness; a growing institution presenting a major challenge to a pharmacist interested in both administration and pharmacology. PO-2

STAFF PHARMACIST—132 bed hospital; salary open; hospital experience preferred. PO-4.

ASSISTANT CHIEF PHARMACIST—eligible for licensure in New Jersey; 350-bed hospital. PO-6.

PHARMACIST—80 bed hospital; full responsibility for pharmacy and central sterile supply services; minimum of one year experience in hospital pharmacy; salary open. PO-17.

ASSISTANT CHIEF PHARMACIST—209 bed general hospital, expanding to 300 beds; 40-hour week; three weeks' vacation; $5,000.00 annually; New Jersey registration required. PO-18.

CHIEF PHARMACIST—to assume full charge of the department; 340 bed hospital, located in New York State. Experience in hospital pharmacy necessary. Salary open. Write PO-20.

PHARMACIST—162 bed hospital located in Ohio; assume complete charge of the department; prefer woman with hospital pharmacy internship; salary open. PO-21.

ASSISTANT CHIEF PHARMACIST—185 bed hospital prefer member of Seventh Day Adventist Church. PO-22.

STAFF PHARMACIST—eligible for licensure in Connecticut; 279 bed hospital; new, modern general hospital located on Long Island Sound, 28 miles from New York City; excellent working conditions and personnel policies. PO-23.

CHIEF PHARMACIST—Kentucky registration required; salary, $6420; 40-hour week; 4 week vacation; non-contributory retirement plan; guaranteed annual salary increases. PO-26.

STAFF PHARMACIST—female preferred; 274 bed hospital and 172 bed maternity hospital; California registration required; salary, $525.00 per month; benefit program represents 17 percent of base salary. PO-27.

CHIEF PHARMACIST—private hospital in South Carolina; to be in complete charge of pharmacy, including purchase and control of drugs; work with medical staff; salary $400.00 to start; retirement program; 41 hour week, 2 week vacation. PO-28.

ASSISTANT CHIEF PHARMACIST AND STAFF PHARMACIST—550 bed general hospital in South Carolina; hospital experience preferred; salary open; 44 hour week; two week vacation. PO-29.

DIRECTOR OF PHARMACY—605 bed hospital located in the East; plan, organize and direct complete pharmaceutical service for this teaching hospital; salary $6,000 to $7,200 per year. PO-30.

ASSISTANT CHIEF PHARMACIST—315 bed community hospital located in New York state; female preferred; 40 hour week; three weeks' vacation; salary open. PO-31.

ASSISTANT CHIEF PHARMACIST—181 bed general hospital; California registration required; 40 hour week; two weeks' vacation; salary $450 to $500 per month. PO-32.

ASSISTANT CHIEF PHARMACIST AND STAFF PHARMACIST—600 bed hospital located in Washington state; assistant chief pharmacist to have M. S. in hospital pharmacy and/or internship in hospital pharmacy; staff pharmacist to have B. S. in pharmacy; 44-hour week; two weeks' vacation; salary open. PO-33.

STAFF PHARMACIST—550 bed general hospital located in Ohio; registration required; 40 hour week; two weeks' vacation; salary $2.50 per hour or based on experience. PO-34.

STAFF PHARMACIST—259 bed general hospital; Virginia registration required; hospital pharmacy experience preferred; 40 hour week, 2 weeks' vacation; salary open. PO-35.

STAFF PHARMACIST—750 bed general hospital located in New York state; B. S. degree required; hospital pharmacy experience desirable but not necessary; 40 hour week; two weeks' vacation; $415.00 per month. PO-36.

STAFF PHARMACIST—manufacturing, dispensing, inventory control and some supervision; registration in Tennessee required; salary $385.00 to $400.00 per month; 44-hour week; paid sick leave. PO-37.

STAFF PHARMACIST—prefer one or more years' experience, with at least one year internship; 42-hour week; 4 week-vacation; salary $450.00 month plus one meal; 660 bed teaching hospital. PO-38.

ASSISTANT CHIEF PHARMACIST—200 bed general hospital located in Tennessee; excellent opportunity for advancement; generous benefits; salary open. PO-39.

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